ANALYSIS OF GLOMERULAR FILTERATION RATE IN NON-ALBUMINURIC TYPE-1 AND TYPE-2 DIABETES MELLITUS IN EARLY DETECTION OF CHRONIC KIDNEY DISEASE

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CHENNAI, TAMILNADU

CERTIFICATE

This is to certify that this dissertation titled **"ANALYSIS OF GLOMERULAR FILTERATION RATE IN NON-ALBUMINURIC TYPE-1 AND TYPE-2 DIABETES MELLITUS IN EARLY DETECTION OF CHRONIC KIDNEY DISEASE"- CROSS-SECTIONAL STUDY** submitted by **Dr.P.SARAVANAN** to the faculty of General Medicine, The Tamilnadu Dr.M.G.R.Medical University, Chennai in partial fulfilment of the requirement for the award of MD degree Branch [GENERAL MEDICINE] is a bonafide research work carried out by him under our direct supervision and guidance.

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This is submitted to **The Tamilnadu Dr.M.G.R.Medical University**, Chennai, in partial fulfilment of the regulations for the award of MD degree Branch [General Medicine].

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INTRODUCTION

Diabetes is a metabolic disorder of multiple causes characterized by chronic hyperglycemia and disorders of carbohydrate, fat, and protein metabolism. It results from defects in insulin secretion (type 1), insulin action (type 2), or combination of these factors. Diabetes has become the most common single cause of end-stage renal disease (ESRD) in India and worldwide. This is due to the fact that diabetes, in particular type 2 diabetes, is increasing in prevalence and patients with diabetes are living longer.

The World Health Organization estimated that there were 135 million diabetics in 1995 and this number would increase to 300 million by the year 2025 {ref:1}. India leads the world with largest number of diabetic subjects earning the dubious distinction of being termed the "diabetes capital of the world". According to the Diabetes Atlas 2006 published by the International Diabetes Federation, the number of people with diabetes in India currently around 40.9 million is expected to rise to 69.9 millions by 2025(Fig : 2) {ref: 3}.

In the 1970s, the prevalence of diabetes among urban Indians was reported to be 2.1 per cent and this has now risen to 12.1 per cent. Moreover, there is an equally large pool of individuals with impaired glucose tolerance , many of whom will develop type 2 diabetes mellitus in the future.{ref: 1}

A national survey of diabetes conducted in six major cities in India in the year 2000 showed that the prevalence of diabetes in urban adults was 12.1%. Prevalence of IGT was also high (14.0%) . (Fig: 1) {ref:2}

Burden of diabetes related complications in India

. A study by Mohan *et al*. in South India showed a prevalence of 34.1% of retinopathy. The CURES Eye study done in India. showed that the overall prevalence of diabetic retinopathy was 17.6 per cent, which was lower when compared to the reports from the West .

Prevalence of PVD in Asian Indians is comparatively low compared with the white population (9.3%){ref:2} The prevalence of peripheral vascular disease was 6.3 per cent among diabetic subjects compared to 2.7 per cent in non-diabetic subjects, and these figures are lower than the prevalence reported in western populations{ref: 3}.

The prevalence of coronary artery disease was 21.4 per cent among diabetic subjects compared to 9.1 per cent in subjects with normal glucose tolerance. The prevalence of CAD in IGT subjects were 14.9 per cent in the same study {ref: 3} Diabetic nephropathy is one of the leading causes of chronic renal failure in India. Among 4837 patients with chronic renal failure seen over a period of 10 years, the prevalence of diabetic nephropathy was 30.3% followed by chronic interstitial nephritis (23%) and chronic glomerulonephritis (17.7%){ref:2}.

A recent population based study reported that the prevalence of overt Nephropathy was 2.2 per cent in Indians while microalbuminuria was present in 26.9 per cent Glycated haemoglobin, duration of diabetes and systolic blood pressure were independently associated with diabetic nephropathy {ref: 3}.

It was estimated that the incidence of renal failure among the south Indian diabetic

patients was 0.69% per annum . A positive association between the *D* allele (*ID* and *DD* genotype) of *ACE* gene polymorphism and diabetic proteinuria in south Indian type 2 diabetic patients was observed which was in agreement with studies in other countries showing such an association. A study had indicated that the risk of CVD was 3-fold higher in nephropathy group than in the nonproteinuric subjects {ref:2}.

. It is estimated that the annual cost of diabetes care would be approximately 90,200 million rupees. The average expenditure per patient per year would be a minimum of Rs 4,500. {ref:2}.

SOCIO-ECONOMIC INFLUENCES

Prevalence of diabetes was found to be lower in the low socio-economic group living in urban areas compared with the high-income group (12.6 vs 24.6% in subjects years). This was probably related to the physical activity of the low income group as most of them were involved in moderate to strenuous physical activity at work. However due to inadequate control of diabetes, the long-term complications such as coronary artery diseases were higher in the low socioeconomic group. This was to some extent related to the higher rates of risk factors such as uncontrolled diabetes,high cholesterol, hypertension, smoking and alcohol consumption. {ref:2}.

FIGURE 1

Recent population based studies showings the prevalence of type 2 diabetes in different parts of India. {ref:3}

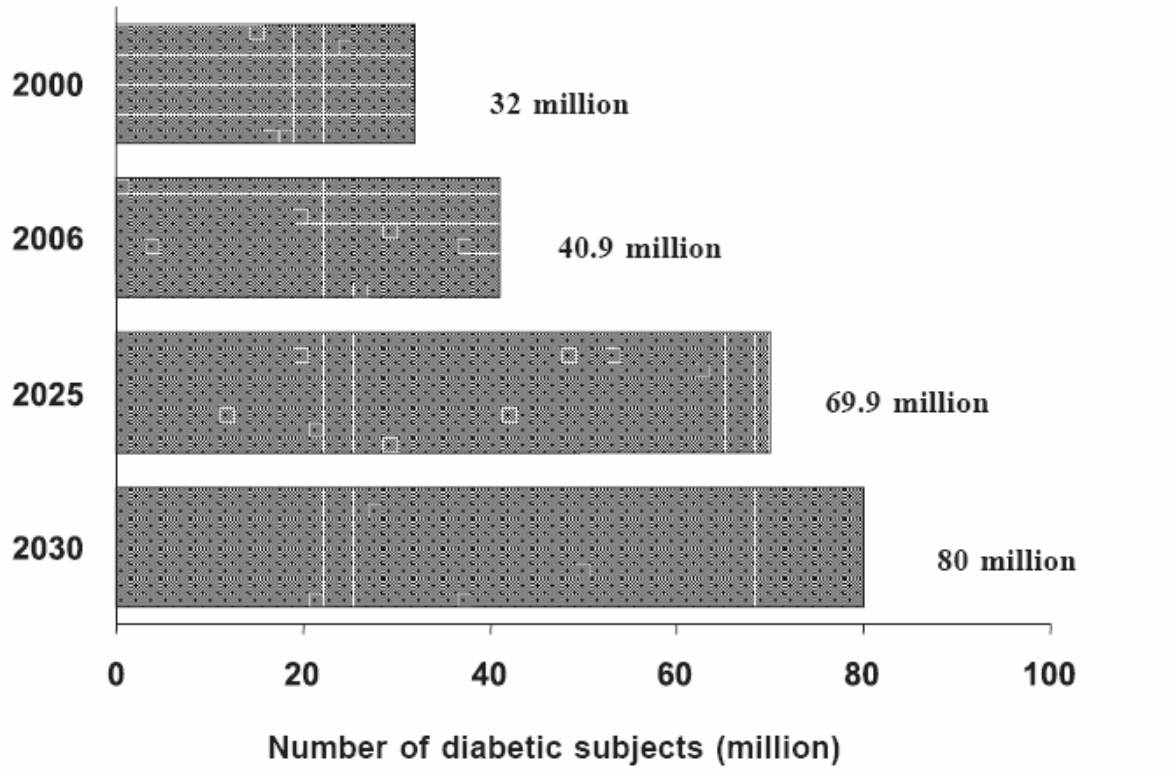

FIGURE : 2

Estimated number of diabetic subjects in India {ref:3}

DIABETIC NEPHROPATHY

Diabetic nephropathy (DN) is one of the most feared complications of both type 1 diabetes mellitus and type 2 diabetes mellitus . Patients who manifest the clinical syndrome of DN (persistent proteinuria and hypertension in association with diabetic retinopathy) are not only destined to develop end-stage renal disease (ESRD), but are also at increased risk of premature cardiovascular disease and all the other complications of diabetes . The development of MA (albumin excretion rate 20–200μg per minute) is typically seen five to 15 years after diagnosis and is associated with a rise in blood pressure, albeit within the 'normal range'. Patients subsequently become macroalbuminuric (albumin excretion rate (AER) >200μg/min), at which time blood pressure is elevated and the other microvascular complications of diabetes emerge. From this point, GFR declines in a linear fashion and, with no intervention, a fall of approximately 10ml/min/year leads to ESRD within 10 years. There is an increasing focus on detecting the earliest stages of DN in routine clinical practice. A typical example is the UK General Practice contract that promotes annual checks of MA in all diabetic subjects and the routine estimation of GFR using the Modification of Diet in Renal Disease (MDRD) equation. In patients who screen positive for either or both of these tests, more aggressive control of blood pressure is recommended, with a focus on inhibition of the renin-angiotensin system {ref:5}.

Keeping all the above-mentioned issues in mind, this study was conducted to estimate GFR with help of MDRD formula in non –albuminuric type 1 and type 2 diabetic individuals for the early detection of diabetic nephropathy in inpatients admitted in department of General Medicine and Diabetology, Government Rajaji hospital, Madurai. .

REVIEW OF LITERATURE

DIABETIC NEPHROPATHY

Diabetic nephropathy (DN) is one of the most common disabling complications of diabetes mellitus. Characteristically, DN is associated with increased proteinuria, hypertension, and progressive loss of renal function. DN can occur in individuals with either type 1 diabetes or type 2 diabetes , and if left untreated frequently leads to progressive renal structural damage and end-stage renal disease (ESRD). Convincing evidence indicates that the rate of progression of both early and late nephropathy in patients with type 1 diabetes, and to a lesser extent in type 2 diabetes, can be attenuated by multiple interventions

Pathogenesis of Diabetic Nephropathy

Although both type 1 and type 2 diabetes mellitus lead to ESRD only about 30% of patients develop clinically overt nephropathy. The majority of subjects with diabetes escape renal failure, and although some histologic damage occurs in their kidneys, their renal function remains essentially normal until they die.

Diabetic nephropathy and hypertension are multifactorial disorders that result from interaction between both environmental and genetic factors .Polymorphisms of genes potentially involved in the genetic predisposition to hypertension, vascular reactivity, and insulin resistance, such as those of the renin-angiotensin system, nitric oxide, aldose reductase, GLUT I, and lipoproteins, have all been investigated in relation to diabetic nephropathy, but studies of candidate genes have, by and large, been inconclusive or, at best, have shown weak associations .

The red blood cell sodium-lithium countertransport system is a cell-membrane cation

transport system whose activity is both genetically determined and increased in essential hypertension and is abnormally high in diabetic patients with proteinuria or microalbuminuria . the pathophysiologic relevance of its abnormalities remains uncertain. Sodium-hydrogen antiport activity is increased in a number of cell types from patients with type 1 diabetes with microalbuminuria and proteinuria, as well as in subjects with hypertension {ref :6}.

THE INSULTS: HYPERGLYCEMIA, HYPERTENSION, AND PROTEINURIA

HYPERGLYCEMIA

There is no doubt that poor glycemic control is associated with diabetic nephropathy. Levels of hemoglobin A_{1c} (HbA_{1c}) are higher in patients with microalbuminuria and macroalbuminuria than in those with normoalbuminuria . In humans, the Diabetes Control and Complications Trial (DCCT), a prospective multicenter randomized clinical trial comparing the effect of intensive and conventional insulin therapy has demonstrated that a sustained improvement in HbA_{1c} reduces the risk of development of diabetic nephropathy . Similarly, the United Kingdom Prospective Diabetes Study (UKPDS) has shown that improved glycemic control is effective in the prevention of microalbuminuria in patients with newly diagnosed type 2 diabetes .

Non enzymatic glycosylation

Sustained hyperglycemia leads to nonenzymatic protein glycation, a posttranslation modification that occurs physiologically but is greatly enhanced in hyperglycemic conditions. These glycated proteins undergo progressive dehydration, cyclization, oxidation, and rearrangement to form advanced glycation end-products (AGEs). Once these AGEs are formed, the reaction is not reversible, and they gradually accumulate over the lifetime of the protein .

AGEs directly alter the structural and functional properties of extracellular matrix proteins. AGE-mediated protein cross-linking increases matrix rigidity and reduces the susceptibility of protein to enzymatic digestion, thus inducing accumulation and thickening, and favors trapping of plasma proteins, such as low-density lipoprotein (LDL) and immunoglobulin G (IgG). In addition, AGEs can elicit a variety of cellular responses by binding to AGE-specific receptors present on many cell types, including mesangial cells and tubular epithelial cells . Interaction of AGE-modified proteins with the AGE receptors serves to degrade AGE proteins but also induces the synthesis and release of cytokines, such as transforming growth factor (TGF-β1), platelet-derived growth factor (PDGF), and insulin-like growth factor (IGF), and results in enhanced production of collagen, laminin, and fibronectin

AGE receptor (RAGE) are also expressed on tubular epithelial cells, and it has recently been reported that RAGE activation can induce tubular epithelial cell transdifferentiation to myofibroblasts, a key event in the development of tubulointerstitial fibrosis. {ref :6}

THE POLYOL PATHWAY

In the renal medullary cells, the primary role of aldose reductase seems to be the formation of sorbitol, an organic osmolyte, in response to the high salinity in the medullary interstitium. It has been argued that, in tissues in which glucose entry into cells is insulin independent, more glucose becomes available for reduction by aldose reductase, resulting in an increased concentration of sorbitol and/or a reduced intracellular concentration of myoinositol.

In the polyol pathway, excess sorbitol is oxidized to fructose by the enzyme fructose dehydrogenase. The increased ratio of NADH/NAD coupled to the oxidation of sorbitol to fructose can result in cellular oxidative stress. Activation of the polyol pathway is more likely to be an epiphenomenon and that other, more central mechanisms are

operating in the pathogenesis of diabetic nephropathy. {ref :6}

GLUCOTOXICITY

Consistent with the finding in clinical studies that hyperglycemia per se plays a key role in the development of diabetic kidney disease, studies on both kidney cells and isolated glomeruli have confirmed that high glucose concentrations directly alter extracellular matrix deposition.

In mesangial cells, high glucose concentrations induce cell hypertrophy and increase gene expression and protein secretion of extracellular matrix components, such as collagen, laminin, and fibronectin . Similarly, levels of type IV and I collagen messenger RNA (mRNA) are enhanced in tubular epithelial cells exposed to high glucose concentrations. High glucose concentrations enhances GLUT 1 expression by mesangial cells, triggering a positive feedback mechanism that may result in progressive damage {ref :6}

HYPERTENSION

There is evidence that hypertension plays a critical role in the progression of diabetic nephropathy. Indeed the development of proteinuria is paralleled in most cases by a gradual rise in systemic blood pressure, and there is a significant correlation between the blood pressure levels and the rate of decline in glomerular filtration rate (65).

In diabetic nephropathy, hypertension is not merely the result of relentless kidney damage; Further, prospective studies in both patients with type 1 and type 2 diabetes and normal albumin excretion have demonstrated that mean arterial pressure levels are significantly higher in those patients who progress to microalbuminuria than in those who do not progress .

Under normal conditions, intraglomerular capillary pressure is tightly regulated by precise adjustments in afferent and efferent arteriolar resistance. Hyperglycemia induces

vasodilatation, and in diabetes there is a marked reduction in afferent and a lesser reduction in efferent arteriolar resistance. This leads to an increase in levels of glomerular capillary pressure and moreover allows ready transmission of any increase in systemic blood pressure to the glomerular capillary network . The metabolic and the hemodynamic insults are thus intimately intertwined in determining altered glomerular hemodynamics. The greater efficacy of angiotensin-converting enzyme (ACE) inhibitors in their antiproteinuric and renoprotective action as compared with other blood pressure-lowering agents has been in part ascribed to the capacity of ACE inhibitors to reduce glomerular capillary pressure by removing the tonic constrictor effect of angiotensin II on the efferent arteriole

when the intraglomerular pressure rises to levels approximating those observed in the diabetic and remnant kidney, glomerular volume increases by about 30%. Glomerular expansion is associated with the stretching of its structural components, including the extracellular matrix and the cellular components.

. Cyclical stretch stimulates the synthesis and deposition of matrix components, such as collagen (I, III, and IV), fibronectin, and laminin, in a manner proportional to the intensity of cellular stretch . Interestingly, although cyclical stretch stimulates collagen synthesis at all glucose concentrations, net collagen accumulation in the medium can be demonstrated only at high glucose levels.. Therefore, the cellular response to a hemodynamic insult can be influenced and exaggerated by high glucose concentration in the milieu{ref :6}.

PROTEINURIA

In diabetic nephropathy and other progressive glomerulopathies, proteinuria is a strong and independent predictor of decline in renal function . Excessive protein overload appears to induce tubulointerstitial damage and hence to contribute to the disease progression . Specifically, the excessive tubular reabsorption of proteins and the consequent accumulation of proteins in tubular epithelial cells induce the release of vasoactive and inflammatory cytokines, such as endothelin-1, osteopontin, and monocyte chemoattractant protein-1 (MCP-1). These factors in turn lead to overexpression of proinflammatory and fibrotic cytokines and infiltration of mononuclear cells, causing injury of the tubulointerstitium and, ultimately, renal scarring and insufficiency . A vicious cycle is then established in which changes in renal hemodynamics, either primary or in response to nephron loss, induce further proteinuria, perpetuating a mechanism of interstitial scarring and loss of more nephrons. The tubular toxicity of protein raises the possibility that the beneficial effects of ACE inhibitors in diabetic renal disease may reflect their potent antiproteinuric action in addition to the reduction of angiotensin II-mediated effects on growth-factor activation and glomerular hemodynamics . Limiting protein excretion and the consequent activation of tubular epithelial cell prosclerotic signals thus appears instrumental in protecting the kidney from further damage {ref :6}

MOLECULAR MEDIATORS

To enhance understanding of the pathogenesis of diabetic nephropathy, a number of studies have examined the cellular and molecular mechanisms of kidney damage. These studies have established the critical concept that the insults of hyperglycemia, high blood pressure, and protein overload converge at the cellular level by using similar molecular signaling pathways and influencing the expression of common cytokines

Transforming Growth Factor-β1

TGF-β is a ubiquitous cytokine that regulates a variety of cellular processes. It exists in three isoforms—TGF-β1, TGF-β2, and TGF-β3—of which TGF-β1 is the best characterized and most highly expressed in the kidney. Glomerular and proximal tubule cells produce TGF-β1 and express both type I and type II TGF-β receptors, which bind to all TGF-β isoforms .

TGF-β1 has important prosclerotic properties and is a potent inducer of cell hypertrophy and apoptosis. *In vitro*, both glomerular mesangial cells and tubular epithelial cells increase their synthesis of collagen, fibronectin, and laminin in response to TGF-β1. Furthermore, TGF-β1 inhibits the synthesis of collagenases and stimulates production of metalloprotease inhibitors. This results in reduced degradation of extracellular matrix and further contributes to accumulation of matrix (85). Finally, *in vivo*, TGF-β1 induces glomerulosclerosis and proteinuria in healthy animals

The importance of TGF-β1 is further highlighted by *in vivo* and *in vitro* studies showing that the three key insults implicated in the pathogenesis of diabetic nephropathy promote the expression of this cytokine. These studies also suggest that TGF-β1 may have a role in the interaction between metabolic and hemodynamic factors in mediating accumulation of extracellular matrix in the diabetic kidney.

High glucose concentrations induce the expression of TGF- β1 in both mesangial and tubular epithelial cells. Further, inhibition of TGF-β1 prevents glucose-induced hypertrophy of mesangial cells and production of extracellular matrix, indicating that these effects are mediated by TGF-β1 via an autocrine mechanism On the other hand, TGF-β1 induces the GLUT1 transporter in mesangial cells and can thereby enhance glucotoxicity . *In vitro*, AGEs induce TGF-β1 gene expression and protein secretion by mesangial cells , and *in vivo* administration of AGEs upregulates TGF-β1 in the kidney .

Further, TGF-β1 mediates, at least in part, stretch-induced overproduction of mesangial matrix . Finally, stretch-induced glucose uptake is also mediated by TGF-β1 . This suggests a key role of TGF-β1 as final common mediator of sclerosis and glucotoxicity in mesangial cells exposed to metabolic and mechanical perturbations.

On the basis of this evidence, it is now generally believed that TGF-β1 is the mediator of a final common pathway leading to sclerosis in diabetic nephropathy. {ref :6}

Connective Tissue Growth Factor

The importance of CTGF in diabetic nephropathy followed its identification by differential cloning as a gene overexpressed in mesangial cells cultured in high glucose concentrations . CTGF is only minimally expressed in the normal kidney, but it is strongly induced in the mesangium in both human and experimental diabetic nephropathy In mesangial cells, CTGF expression is induced by high glucose concentrations, mechanical stretch, and TGF-β1 . Furthermore, CTGF is a crucial downstream mediator of TGF-β1 signaling, but it appears to mediate selectively the TGF-β1 profibrotic effect of increased production of extracellular matrix, whereas it does not have antiproliferative and immunosuppressive activity .

Specifically, CTGF appears to enhance IGF-1 prosclerotic effects, increasing the binding of TGF-β1 to its receptors, and to prevent VEGF binding to the KDR receptor . This suggests that CTGF may play a role in the pathogenesis of diabetic nephropathy not only by acting directly on mesangial cells but also by modulating the activity of other cytokines implicated in the pathogenesis of the glomerular damage{ref :6}

Growth Hormone and Insulin-like Growth Factor

IGF-1 stimulates endothelial nitric oxide synthase (eNOS) activity *in vitro* in endothelial cells and induces vasodilation *in vivo*, and this provides a potential link between IGF-1 and glomerular hyperfiltration and hypertrophy . In a high-glucose milieu, IGF-1 induces the proliferation of mesangial cells, which also may contribute to the glomerular hypertrophy of early diabetes. In mesangial cells, IGF-1 increases both matrix production and GLUT1 activity , suggesting a role of IGF-1 in glomerulosclerotic process. {ref :6}

Vascular Endothelial Growth Factor

Insults relevant to diabetes, such as high glucose, AGEs, mechanical stretch, angiotensin II, IGF-1, and TGF-β1, have been shown to induce VEGF production *in vitro* in mesangial cells Moreover, in glomerular epithelial cells, high glucose induces VEGF in a TGF-β-1-dependent manner, and stretch stimulates both production of VEGF and expression of VEGF receptor .

Both VEGF and VEGF receptors are overexpressed in the glomeruli *in vivo* in experimental diabetes and in patients with type 2 diabetes , and plasma VEGF levels are raised in patients with type 1 diabetes with nephropathy

VEGF potently stimulates eNOS expression and activity in cultured endothelial cells , and VEGF blockade normalizes eNOS expression by glomerular capillaries providing a potential link between VEGF and both glomerular hyperfiltration and hypertrophy in diabetes. {ref :6}

Angiotensin II

ACE inhibitors appear to have a greater efficacy than other blood pressure-lowering agents in their antiproteinuric and renoprotective action. This has been classically ascribed to their effect on glomerular hemodynamics, as suggested by treatments that, by

interfering with angiotensin II action, normalize glomerular capillary pressure in diabetic rats .

In particular, angiotensin II can directly induce matrix deposition via a TGF-β1-dependent mechanism in both mesangial and tubular cells .High glucose induces production of angiotensin II in mesangial cells and stretch magnifies the response of mesangial cells to angiotensin II by upregulating the angiotensin II receptor AT1 .Therefore, in mesangial cells the deleterious effects of hyperglycemia and high intraglomerular pressure may result from an enhanced production of and responsiveness to angiotensin II. In glomerular epithelial cells, angiotensin II induces apoptosis via a TGF-β1-dependent mechanism .

In isolated glomeruli, angiotensin II increases glomerular permeability to protein and impairs the size-selective function of the glomerular filter. It thus appears that the efficacy of ACE inhibitors and angiotensin II receptor antagonists is due not simply to inhibition of the hemodynamic effects of angiotensin II but also to direct blockade of the cytokine and growth factor action of angiotensin II. {ref :6}

TRANSCRIPTION FACTORS AND INTRACELLULAR SIGNALING PATHWAYS

. It is critical to identify the transcription factor or factors implicated in matrix overexpression in diabetic nephropathy and to establish which intracellular signaling pathways are involved in induction or activation of these transcription factors.

Nuclear Factor-κB

The transcription factor NF-κB plays a pivotal role in early gene responses by promoting the synthesis of mRNA for various cell-adhesion molecules and cytokines. NF-κB is important in cell survival, and its inhibition has been causally related to apoptosis. High

glucose, AGEs, angiotensin II, and stretch potently induce NF-κB activation mainly via formation of reactive oxygen species and activation of PKC , providing potential cellular mechanisms of NF-κB activation in the diabetic kidney. NF-κB is believed to play a key role in proteinuria-induced tubulointerstitial damage in diabetes. Both ACE inhibitors and statins are potent NF-κB inhibitors, and their renoprotective action may be related, at least in part, to the suppression of NF-κB activity. {ref :6}

Fos, Jun, and the AP-1 Transcription Factor

c-*fos* and c-*jun* are two highly conserved proto-oncogenes. c-Fos and c-Jun proteins combine in homo/heterodimers (c-Fos/c-Jun, c-Jun/c-Jun) to form the AP-1 transcription complex, which binds to and induces genes with AP-1-binding consensus sequences in their promoter regions . Genes encoding for TGF-β1, fibronectin, and laminin contain AP-1-binding sites in their promoters; thus, AP-1 may stimulate their transcription and induce expression of extracellular matrix protein genes via direct and indirect mechanisms .

High glucose concentrations and mechanical stretch induce expression of c-*fos* and c-*jun* in mesangial cells and is associated with increased transcription of target extracellular matrix protein genes via formation of the AP-1 transcription factor.

Therefore, the AP-1 transcription factor plays an important role in the cascade leading to excess deposition of matrix deposition. {ref :6}

Intracellular Signaling Pathways

PROTEIN KINASE C

PKC, a family of ubiquitous serine-threonine kinases, is important in the transduction of many extracellular signals.. Both classical and novel PKC isoforms are activated by diacylglycerol (DAG) . PKC induces expression of c-*fos* and c-*jun* , thus, PKC can be

proposed as a potential candidate responsible for the increased AP-1 expression seen in diabetic nephropathy..

In diabetes, DAG levels are increased and PKC is activated in a variety of tissues, including kidney glomeruli . High glucose concentrations lead to *de novo* DAG synthesis, which is then responsible for PKC activation . It is interesting that activation of the DAG-PKC pathway in diabetic animals is maintained chronically, and this supports the hypothesis of a role of this system in the pathogenesis of chronic diabetic complications. Furthermore, glycated products and activation of the polyol pathway can also activate the DAG-PKC cascade, suggesting that the activation of DAG-PKC may be a common downstream mechanism by which multiple by-products of glucose exert their adverse effects . PKC is also a crucial downstream mediator of TGF-β1, angiotensin II, VEGF, and cyclic stretch signaling, indicating that PKC activation is a key intracellular target of both metabolic and hemodynamic insults . {ref :6}

.**MITOGEN-ACTIVATED PROTEIN KINASES**

Extracellular signal-related kinases (ERK), stress-activated protein kinases (JNK), and p38 kinases (p38) are members of the mitogen-activated protein kinase (MAPK) superfamily. These kinases constitute functionally distinct, but structurally related, transduction pathways by which extracellular signals are transmitted to the nucleus to regulate gene expression. Specifically, MAPKs are activated by phosphorylation at specific threonine and tyrosine residues in response to various cytokines and extracellular stresses. Activated MAPKs translocate to the nucleus, where they phosphorylate and transactivate specific transcription factors, which regulate the expression of c-*fos* and c-*jun* genes. Thus, MAPKs may influence extracellular matrix protein genes and TGF-β1

expression via an AP-1-dependent mechanism .

Human mesangial cells exposed to stretch show rapid activation of p38, resulting in a direct and independent production of fibronectin and TGF-β1; the latter in turn contributed to the maintenance of long-term p38 activation in a vicious cycle, resulting in the perpetuation of fibronectin accumulation {ref :6}

Clinical definition of diabetic nephropathy

- Progressive rise in urine albumin excretion.
- Progressive rise in blood pressure.
- Eventual decline in glomerular filtration rate and end stage renal failure.
- In the presence of diabetic retinopathy.
- Accompanied by progressive rise in cardiovascular risk.

Diabetic nephropathy is a clinical syndrome characterized by persistent albuminuria (>300 mg/d or >200 mcg/min) that is confirmed on at least 2 occasions 3-6 months apart.

TABLE -- Pathology of Diabetic Nephropathy in Patients with Type 1 Diabetes and Proteinuria

ALWAYS PRESENT	OFTEN OR USUALLY PRESENT	SOMETIMES PRESENT
Glomerular basement membrane thickening	Kimmelstiel-Wilson nodules (nodular glomerulosclerosis) global glomerular sclerosis focal-segmental glomerulosclerosis , tubular glomeruli	Hyaline "exudative" leisons (subendothelial)
Tubular basement membrane thickening		Capsular drops
Mesangial expansion with predominance of increased mesangial matrix (diffuse glomerulosclerosis)	Foci of tubular atrophy	Atherosclerosis
Interstitial expansion with predominance of increased extracellular matrix material		Glomerular microaneurysms
Increased glomerular basement membrane, tubular basement membrane, and Bowman capsule staining for albumin and IgG	Afferent and efferent arteriolar hyalinosis	

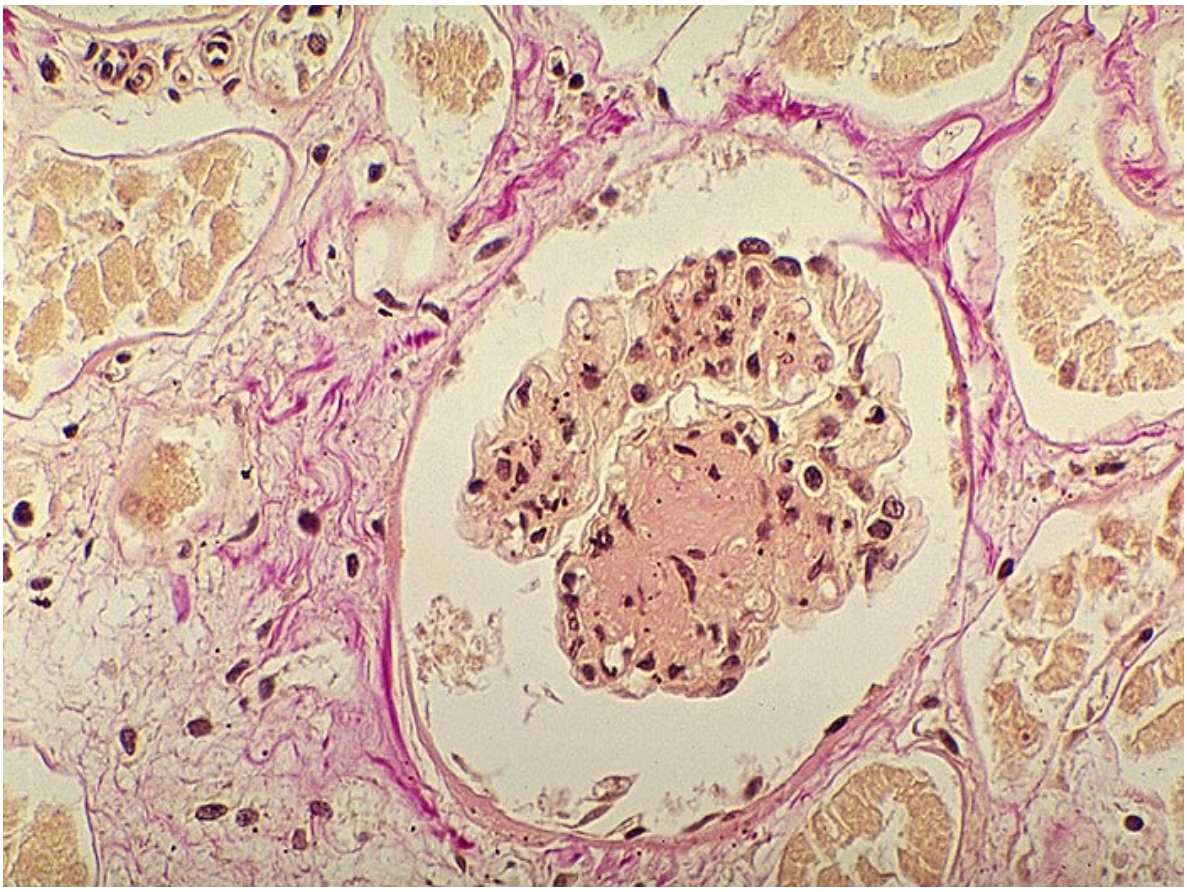

Figure 3. **Nodular glomerulosclerosis (diabetic nephropathy)**

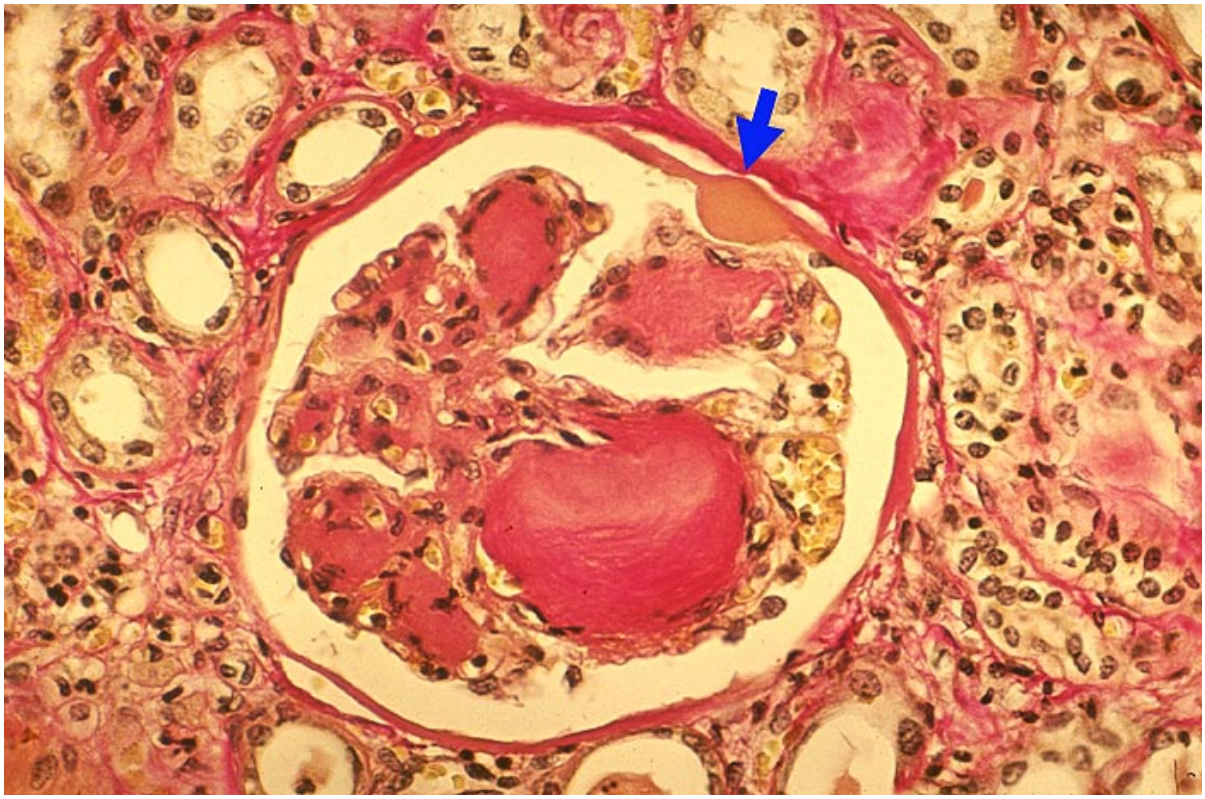

Figure 4. **Nodular glomerulosclerosis (diabetic nephropathy) capsular drop. Nodular swelling of the mesangium**.

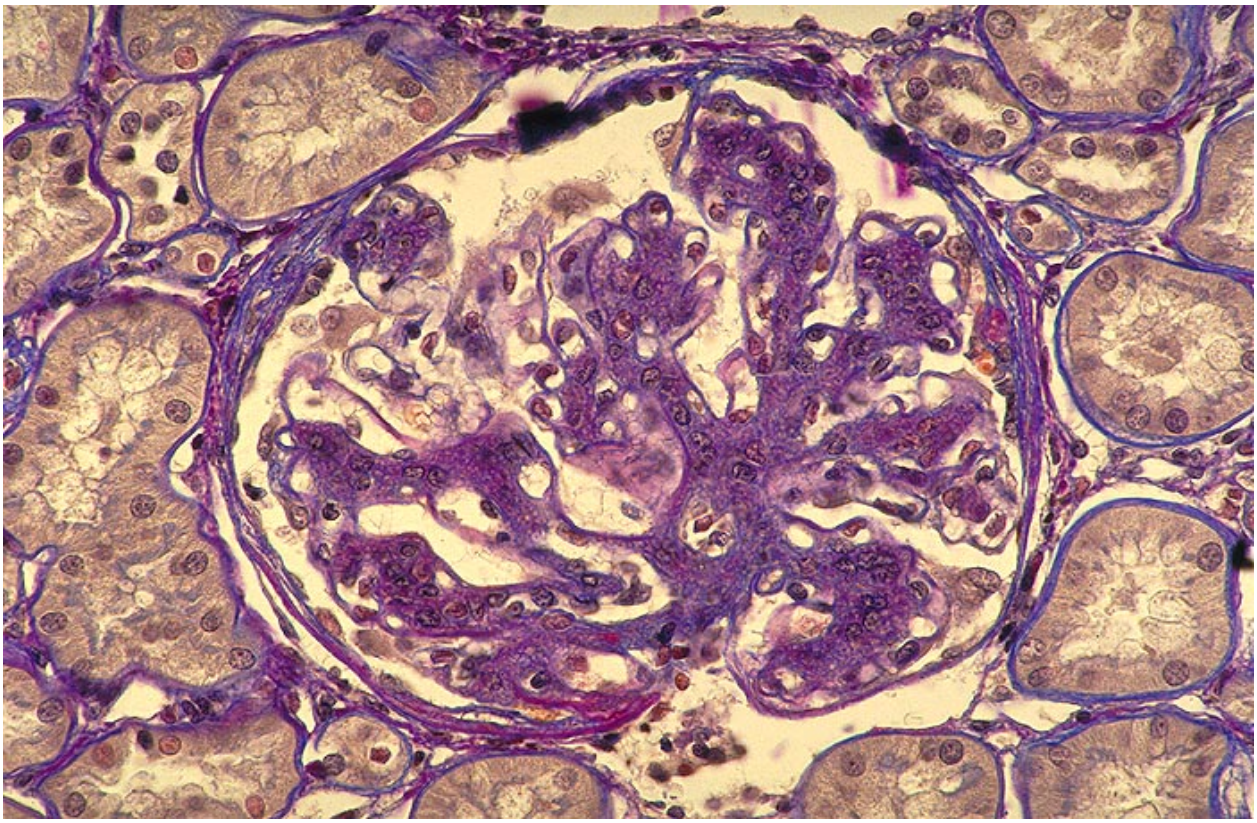

Figure .5 Diffuse glomerulosclerosis (diabetic nephropathy)

NATURAL HISTORY OF NEPHROPATHY

Normoalbuminuria

Approximately one third of type 1 diabetic patients will have a GFR above the upper normal range of age-matched healthy nondiabetic subjects. The degree of hyperfiltration is less in type 2 diabetic patients and reported lacking in some studies. Four factors regulate GFR

.

Longitudinal studies suggest that hyperfiltration is a risk factor for subsequent increase in urinary albumin excretion and development of diabetic nephropathy in type 1 diabetic patients but conflicting results have also been reported. The prognostic significance of hyperfiltration in type 2 diabetic patients is still debated. Six prospective cohort studies investigating normoalbuminuric type 1 and type 2 diabetic patients for 4 to 10 years revealed that minimal elevation of urinary albumin excretion, poor glycemic control, hyperfiltration, elevated arterial blood pressure, retinopathy, and smoking contribute to the development of persistent microalbuminuria and overt diabetic nephropathy Because several of those risk factors are modifiable, intervention is feasible{BRENNER}

Microalbuminuria

In addition to hyperglycemia, many other factors can induce microalbuminuria in diabetic patients such as hypertension, massive obesity, heavy exercise, various acute or chronic illnesses, and cardiac failure

Alterations in glomerular pressure and flow influence both the diffusive and the

convecting driving forces for transglomerular passage of proteins Reduction in the negatively charged moieties of the glomerular capillary wall, particularly sialic acid and heparan sulfhate, have been suggested, but not confirmed Changes in podocyte number and morphology have been implicated in the pathogenesis of proteinuria and progression of diabetic kidney disease Filtration fraction is presumed to reflect the glomerular hydraulic pressure, and microalbuminuric type 1 diabetic patients have elevated filtration both at rest and during exercise compared to normal controls

Prospective studies have demonstrated that GFR remains stable at normal or supranormal levels for at least 5 years if clinical nephropathy does not develop Nephromegaly is still present and even more pronounced in microalbuminuric compared to normoalbuminuric type 1 diabetic patients.

Changes in tubular function take place early in diabetes and are related to the degree of glycemic control. The proximal tubular reabsorption of fluid, sodium, and glucose is enhanced.[208] This process could diminish distal sodium delivery and thereby stimulate a tubuloglomerular feedback-mediated enhancement of GFR{BRENNER}

Extrarenal Complications in Diabetic Nephropathy

Diabetic retinopathy is present in virtually all type 1 diabetic patients with nephropathy, whereas only 50% to 60% of proteinuric NIDDM patients suffer from retinopathy. Absence of retinopathy should require further investigation for nondiabetic glomerulopathies.. Blindness due to severe proliferative retinopathy or maculopathy is approximately five times greater in type 1 and type 2 diabetic patients with nephropathy compared to normoalbuminuric patients.Macroangiopathy, for example, stroke, carotid artery stenosis, CHD, and peripheral vascular disease are two to five times more common in nephropathic patients..

Peripheral neuropathy is present in almost all patients with advanced nephropathy. Foot ulcers with sepsis leading to amputation occur frequently (>25%), probably due to a combination of neural and arterial disease.

. over half of the patients with advanced nephropathy had symptoms of autonomic neuropathy: gustatory sweating, impotence, postural hypotension, and diarrhea. Diabetic cystopathy is also a frequent (>30%) problem in these patients. {BRENNER}

Diabetic Nephropathy

Diabetic nephropathy is a clinical syndrome characterized by persistent albuminuria (>300 mg/24 hours), a relentless decline in GFR, and raised arterial blood pressure. While albuminuria is the first sign, peripheral edema is the first symptom of diabetic nephropathy. Fluid retention is frequently observed early in the course of this kidney disease, that is, at a stage with well-preserved renal function and only slight reduction in serum albumin. A recent study suggests that capillary hypertension, increased capillary surface area, and reduced capillary reflection coefficient for plasma proteins contribute to the edema formation, whereas the washout of subcutaneous interstitial protein tends to prevent the progressive edema formation in diabetic nephropathy.

Most studies dealing with the natural history of diabetic nephropathy have demonstrated a relentless, often linear but highly variable rate of decline in GFR ranging from 2 to 20 mL/minute/year, with a mean of 12 mL/minute/year .Type 2 diabetic patients suffering from nephropathy display the same degree of loss in filtration power and in variability of GFR. Morphologic studies in both type 1 and type 2 diabetic patients have demonstrated a close inverse correlation between the degree of glomerular and tubulointerstitial lesions on the one side and the GFR level on the other side.. A reduction in the number of restrictive pores leading to loss of ultrafiltration capacity (Kf) and impairment of

glomerular barrier size-selectivity leading to progressive albuminuria and IgGuria in diabetic nephropathy.

Impaired or abolished renal autoregulation of GFR and RPF as demonstrated in type 1 and type 2 diabetic patients with nephropathy contribute to increase vulnerability to hypertension or ischemic injuries of glomerular . More severe diabetic glomerulopathy lesions have been documented both during development and progression of renal disease in type 2 diabetic patients with the D allele.Furthermore, microalbuminuric type 1 patients carrying the D allele have an increased progression of diabetic glomerulopathy. Nondiabetic glomerulopathy is very rare in proteinuric type 1 diabetic patients, whereas this condition is common in proteinuric type 2 diabetic patients without retinopathy. A prevalence of biopsies with normal glomerular structure or nondiabetic kidney diseases of approximately 30% was demonstrated.

Systemic blood pressure elevation to a hypertensive level is an early and frequent phenomenon in diabetic nephropathy. Furthermore, nocturnal blood pressure elevation ("non-dippers") occurs more frequently in type 1 and type 2 diabetic patients with nephropathy {BRENNER}

Changing natural history of diabetic nephropathy

Microalbuminuria generally appears within 5–15 years' duration of diabetes. Without specific intervention, over approximately a further 10 years, dipstick positive or conventional proteinuria is present. when, untreated, there is a progressive decline in glomerular filtration over a further 10 years, until end stage renal failure is reached..

The cumulative incidence of microalbuminuria and proteinuria in several more recent studies is 35%–40% and 25% respectively after 25–30 years of diabetes {ref :10}

In white individuals, the development of diabetic nephropathy follows a similar course to

that in type 1 diabetes..

In non-white individuals, the cumulative risk of nephropathy is almost certainly higher and the disease may develop more rapidly than in white people

An estimated 5% to 15% of DM 2 cases also progress through the five stages of diabetic nephropathy (DN), but the timeline is not as clear. Some patients advance through the stages very quickly. {ref :10}

Type 1 and white type 2 diabetic patients

Microalbuminuria develops at a rate of 2%–3% per annum.

The cumulative incidence of microalbuminuria is ~50% over a life time of diabetes.

One third of microalbuminuric patients progress to proteinuria.

Almost all proteinuric patients develop end stage renal disease or die prematurely of cardiovascular disease.

Long duration patients may not be protected.

Non-white type 2 diabetic patients

Microalbuminuria develops at a rate of ~4% per annum.

The cumulative incidence of microalbuminuria is ~50% at 20 years' duration of diabetes.

Progression from microalbuminuria to proteinuria and end stage renal disease may occur faster than in type 1 diabetes {ref :10}

CLINICAL STAGING OF DIABETIC NEPHROTHY

Stage 1 (very early diabetes) Increased demand upon the kidneys is indicated by an above-normal glomerular filtration rate (GFR)

Stage 2 (developing diabetes) The GFR remains elevated or has returned to normal, but glomerular damage has progressed to significant microalbuminuria (small but above-normal level of the protein albumin in the urine). Patients in stage 2 excrete more than 30 mg of albumin in the urine over a 24-hour period

Stage 3 (overt, or dipstick-positive diabetes) Glomerular damage has progressed to clinical albuminuria. The urine is "dipstick positive," containing more than 300 mg of albumin in a 24-hour period. (high blood pressure) typically develops during stage 3.

Stage 4 (late-stage diabetes) Glomerular damage continues, with increasing amounts of protein albumin in the urine. The kidneys' filtering ability has begun to decline steadily, and blood urea nitrogen (BUN) and creatinine (Cr) has begun to increase. The glomerular filtration rate (GFR) decreases about 10% annually. Almost all patients have hypertension at stage 4.

Stage 5 (end-stage renal disease, ESRD) GFR has fallen to approximately 10 milliliters per minute (<10 mL/min) and renal replacement therapy (i.e., hemodialysis, peritoneal dialysis, kidney transplantation) is needed.

Progression through these five stages is rather predictable because the onset of DM 1 can be identified, and most patients are free from age-related medical problems. {ref :10}

From the literature search a number of potential risk factors were. A variety of potential risk factors were assessed in studies of longitudinal design. These were:

blood glucose levels, blood pressure levels, smoking , lipids, body mass index ,age ,sex , baseline albumin excretion , duration of diabetes , retinopathy.

Three other risk factors; homocysteine, family history, race were identified only by cross sectional studies.{ref:11}

TABLE Risk Factors and Markers for Development of Nephropathy in Type 1 and Type 2 Diabetic Patients

RISK FACTORS / MARKERS	TYPE 1	TYPE2
Normoalbuminuria (above median)	+	+
Microalbuminuria	+	+
Sex	M > F	M > F
Familial clustering	+	+
Predisposition to arterial hypertension	±	+
Increased sodium/lithium counter transport	±	--
Ethnic conditions	+	+
Onset of IDDM before age 20 yr	+	?
Glycemic control	+	+
Hyperfiltration	±	±
Prorenin	+	?
Smoking	+	?
Cholesterol	+	+
Presence of retinopathy	+	+

{Ref:Brenner}

SCREENING FOR DIABETIC NEPHROPATHY AND MONITORING RENAL FUNCTION

Clinical Practice Guidelines for Diabetes and Chronic Kidney Disease (CKD) {REF;13}

Screening and Diagnosis of Diabetic Kidney Disease (DKD)

CKD in patients with diabetes may or may not represent DKD. In the absence of an established diagnosis, the evaluation of patients with diabetes and kidney disease should include investigation into the underlying cause(s).

Patients with diabetes should be screened annually for DKD. Initial screening should commence:

- 5 years after the diagnosis of type 1 diabetes; or
- From diagnosis of type 2 diabetes.

Screening should include:

- Measurements of urinary albumin-creatinine ratio (ACR) in a spot urine sample;
- Measurement of serum creatinine and estimation of glomerular filtration rate (GFR).

An elevated ACR should be confirmed in the absence of urinary tract infection with 2 additional first-void specimens collected during the next 3 to 6 months.

- Microalbuminuria is defined as an ACR between 30-300 mg/g.
- Macroalbuminuria is defined as an ACR >300 mg/g.
- 2 of 3 samples should fall within the microalbuminuric or macroalbuminuric range to confirm classification.

In most patients with diabetes, CKD should be attributable to diabetes if:

- Macroalbuminuria is present; or

- Microalbuminuria is present
    - In the presence of diabetic retinopathy
    - In type 1 diabetes of at least 10 years' duration

Other cause(s) of CKD should be considered in the presence of any of the following circumstances:

- Absence of diabetic retinopathy
- Low or rapidly decreasing GFR
- Rapidly increasing proteinuria or nephrotic syndrome
- Refractory hypertension
- Presence of active urinary sediment
- Signs or symptoms of other systemic disease; or
- >30% reduction in GFR within 2-3 months after initiation of an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-receptor blocker (ARB).

.

As ACR may be elevated with conditions other than diabetic nephropathy, such as recent major exercise , fever , urinary tract infection, congestive heart failure , acute severe elevations of blood pressure (BP) or blood glucose (BG) , or menstruation, screening for microalbuminuria should be delayed in the presence of these conditions.

Creatinine clearance, an estimate of the kidney's ability to filter toxins from the blood, should be determined by a formula such as the Cockcroft-Gault formula or Modification of Diet in Renal Disease (MDRD) formula rather than by serum creatinine, which may falsely indicate that a person's renal function is normal .

Cross sectional studies appear to show that cystatin C rises out with the reference range before serum creatinine and correlates better with iohexol glomerular filtration rate than

creatinine clearance or glomerular filtration rate calculated by the Cockcroft-Gault equation. Cystatin C is assayed by an automated immunoturbidimetric assay, so that it would be applicable to routine clinical practice if longitudinal studies confirm its promise**.**

Management of Hyperglycemia and General Diabetes Care in CKD

Hyperglycemia, the defining feature of diabetes, is a fundamental cause of vascular target-organ complications, including kidney disease. Intensive treatment of hyperglycemia prevents DKD and may slow progression of established kidney disease.

Target hemoglobin A_{1c} (HbA_{1c}) for people with diabetes should be <7.0%, irrespective of the presence or absence of CKD.

Management of Hypertension in Diabetes and CKD

Most people with diabetes and CKD have hypertension. Treatment of hypertension slows the progression of CKD.

Hypertensive people with diabetes and CKD stages 1-4 should be treated with an ACE inhibitor or an ARB, usually in combination with a diuretic.

Target blood pressure in diabetes and CKD stages 1-4 should be <130/80 mmHg.

Management of Dyslipidemia in Diabetes and CKD

Dyslipidemia is common in people with diabetes and CKD. The risk of cardiovascular disease (CVD) is greatly increased in this population. People with diabetes and CKD should be treated according to current guidelines for high-risk groups.

Target low-density lipoprotein cholesterol (LDL-C) in people with diabetes and CKD stages 1-4 should be <100 mg/dL; <70 mg/dL is a therapeutic option.

People with diabetes, CKD stages 1-4, and LDL-C $\geq$100 mg/dL should be treated with a

statin.

Treatment with a statin should not be initiated in patients with type 2 diabetes on maintenance hemodialysis therapy who do not have a specific cardiovascular indication for treatment.

Nutritional Management in Diabetes and CKD

Management of diabetes and CKD should include nutritional intervention. Dietary modifications may reduce the progression of CKD.

Target dietary protein intake for people with diabetes and CKD stages 1-4 should be the recommended daily allowance (RDA) of 0.8 g/kg body weight per day.

Management of Albuminuria in Normotensive Patients With Diabetes and Albuminuria as a Surrogate Marker

Normotensive people with diabetes and macroalbuminuria should be treated with an ACE inhibitor or an ARB.

Treatment with an ACE inhibitor or an ARB may be considered in normotensive people with diabetes and microalbuminuria.

Albuminuria reduction may be considered a treatment target in DKD

Multifaceted Approach to Intervention in Diabetes and CKD

The care of people with diabetes and CKD should incorporate a multifaceted approach to intervention that includes instruction in healthy behaviors and treatments to reduce risk factors.

Target body mass index (BMI) for people with diabetes and CKD should be within the normal range (18.5-24.9 kg/m^2).

Diabetes and CKD in Special Populations

Screening and interventions for diabetes and CKD should focus on populations at greatest risk.

Although management of diabetes and CKD in special populations should follow the same principles as management in the majority population, there are special considerations in the treatment of children, adolescents, and the elderly.

Population-based interventions may be the most cost-effective means for addressing the burden of CKD in special populations. Implementation and evaluation of population-based interventions should take into account the heterogeneity of the populations at risk.

Specialists in high-risk pregnancy and kidney disease should co-manage pregnancy in women with diabetes and CKD.

Treatment of DKD with renin-angiotensin system (RAS) inhibitors before pregnancy may improve fetal and maternal outcomes, but these medicines should be discontinued as soon as a menstrual period is missed or after a positive pregnancy test.

Insulin should be used to control hyperglycemia if pharmacological therapy is necessary in pregnant women with diabetes and CKD.

Behavioral Self-Management in Diabetes and CKD

Self-management strategies should be key components of a multifaceted treatment plan with attention to multiple behaviors:

- Monitoring and treatment of glycemia
- Blood pressure
- Nutrition
- Smoking cessation
- Exercise
- Adherence to medicines

AIMS AND OBJECTIVES

TO ANALYSE GLOMERULAR FILTERATION RATE IN NON ALBUMINURIC TYPE 1 AND TYPE 2 DIABETES MELLITUS PATIENTS, DEFINED AS GLOMERULAR FILTERATION RATE LESS THAN 90 ML/MIN PER 1.73M 2 BODY SURFACE AREA FOR EARLY DETCTION OF CHRONIC KIDNEY DISEASE .

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MATERIALS AND METHODS

Setting : All patients of type 1 and type 2 diabetes mellitus admitted in Department of Medicine and Department of Diabetology GRH, Madurai.

Collaborating Departments **:** Department of Nephrology
Madurai Medical College
Madurai.
Department of Diabetology
Madurai Medical College
Madurai
Department of Biochemistry
Madurai Medical College
Madurai

Design of the study **:** Cross-sectional study

Period of study **:** 01.12.2005 – 30.09.2007

Sample size **:** Type 1 Diabetes mellitus- 25
: Type 2 Diabetes mellitus - 161

Ethical committee approval **:** Obtained

Consent **:** Informed consent was obtained

Financial support **:** Nil

Conflict of interest **:** Nil

DEFINITION OF DIABETES MELLITUS

The criteria for the diagnosis of diabetes are as follows:

Symptoms of diabetes associated with

a. Random plasma glucose concentration ≥ 200 mg/dl

b. Fasting plasma glucose ≥ 126 mg/dl

c. 2 hr plasma glucose ≥ 200 mg/dl during a 75 g OGTT.

For asymptomtic individuals with any one of the above values, a 75 g OGTT is required to confirm the diagnosis. Random is defined as any time of day with out regard to time since the last meal. The classic symptoms of diabetes include polyuria, polydipsia, Polyphagia and unexplained weight loss, Fasting is defined as no caloric in take for at least eight hours

DEFINITION OF RETINOPATHY

The diabetic retinopathy was classified as absent retinopathy, background retinopathy, and proliferative retinopathy and was assessed by fundoscopy.(fig.6 to fig.14)

QUANTIFICATION OF ALBUMINURIA

	Urine collection method	**Normal**	**Microalbuminuria**	**Albuminuria or clinical proteinuria**
Total Protein	24-Hour Excretion (varies with method)	<300 mg/day	NA	>300 mg/day
	Spot Urine Dipstick	<30 mg/dL	NA	>30 mg/dL
	Spot Urine Protein-to-Creatinine Ratio (varies with method)	<200 mg/g	NA	>200 mg/g

Ref ;Schrier, Robert W. Title: Diseases of the Kidney & Urinary Tract, 8th Edition

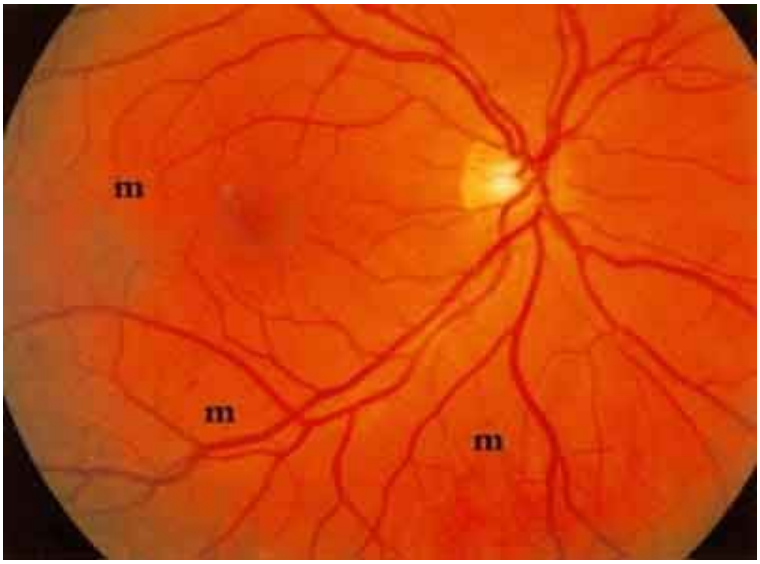

Figure.6 MINIMAL NON-PROLIFERATIVE DIABETIC RETINOPATHY (NPDR) -- FEW SCATTERED MICROANEURYSMS (m) ONLY, THE REMAINDER OF THE FUNDUS IS NORMAL.

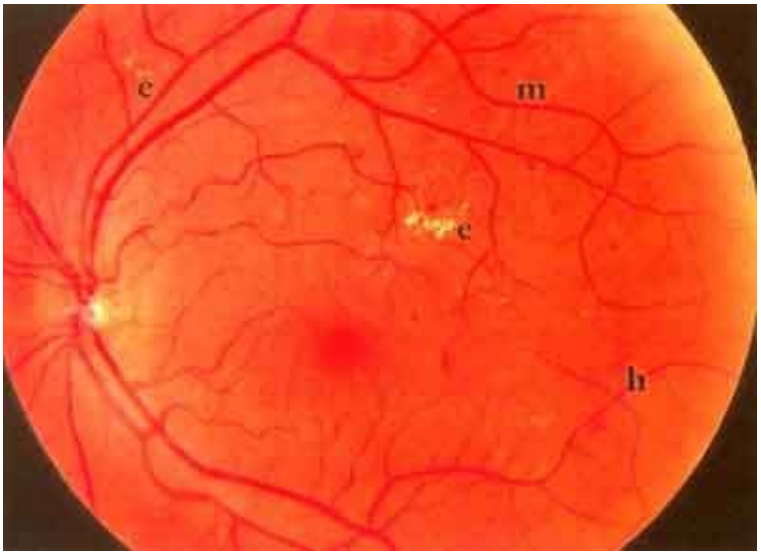

Figure.7 MILD NON-PROLIFERATIVE DIABETIC RETINOPATHY -- MICROANEURYSMS (m) AND DOT HAEMORRHAGES (h). ALSO DEMONSTRATES MACULAR OEDEMA WITH A SMALL AMOUNT OF LIPID EXUDATE (e) -- NOT CLINICALLY SIGNIFICANT.

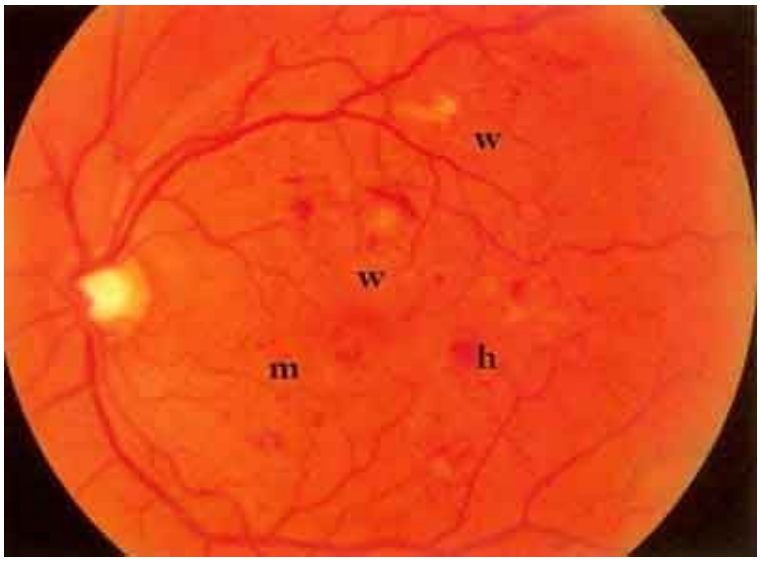

Figure.8 MODERATE NON-PROLIFERATIVE DIABETIC RETINOPATHY -- COTTON WOOL SPOTS (w) RETINAL HAEMORRHAGES (h) AND MICROANEURYSMS (m)

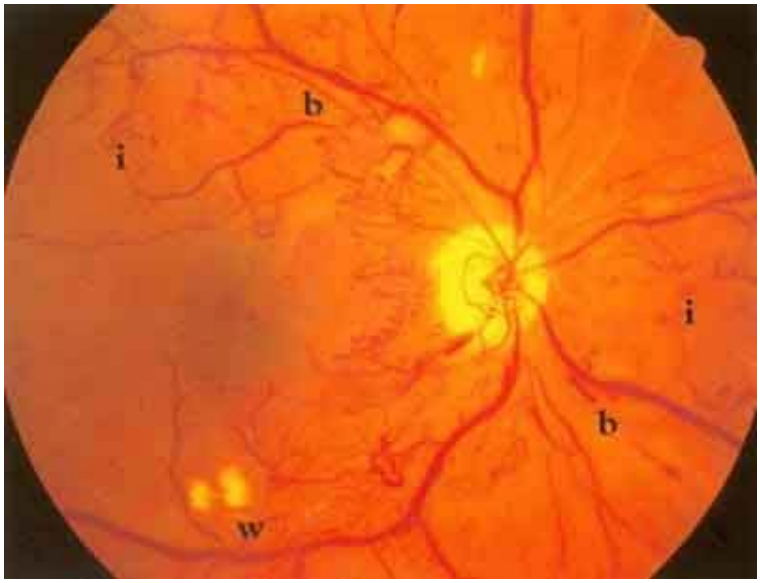

Figure.9 SEVERE NON-PROLIFERATIVE DIABETIC RETINOPATHY -- INTRARETINAL MICROVASCULAR ABNORMALITIES OR IRMA (i) VENOUS READING (b) OR VENOUS CALIBER CHANGES, WIDESPREAD RETINAL ISCHAEMIA AND COTTON WOOL SPOTS (w) -- BEGINNING OF NEW VESSEL ON OPTIC DISC.

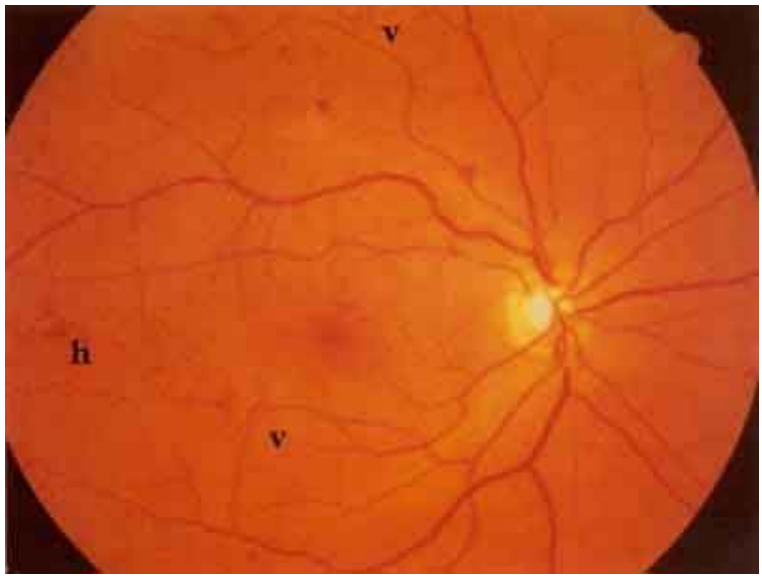

Figure.10 PROLIFERATIVE DIABETIC RETINOPATHY -- PERIPHERAL NEW VESSEL (v), RETINAL HAEMORRHAGES (h) AND NO VITREOUS OR PRE-RETINAL HAEMORRHAGE -- NOTE LACK OF OTHER RETINOPATHY FEATURES

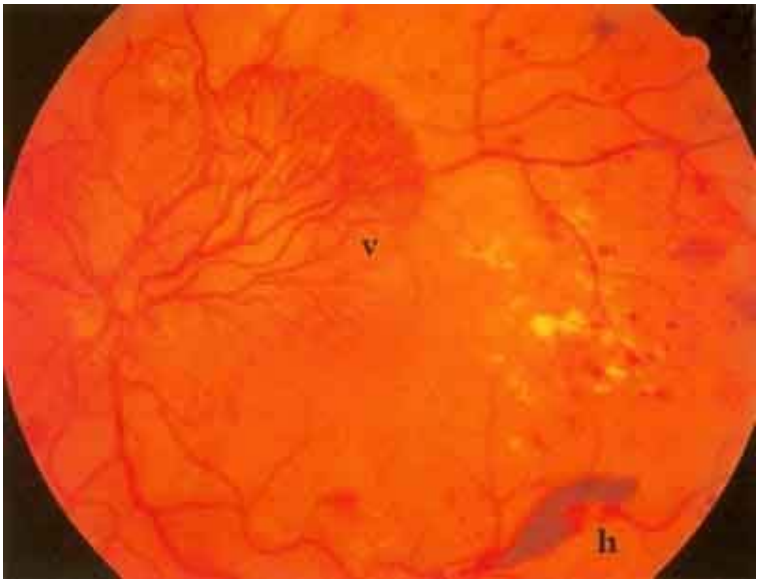

Figure.11 HIGH-RISK PROLIFERATIVE DIABETIC RETINOPATHY -- LARGE FROND OF DISC NEW VESSEL (v) AND PRE RETINAL HAEMORRHAGE

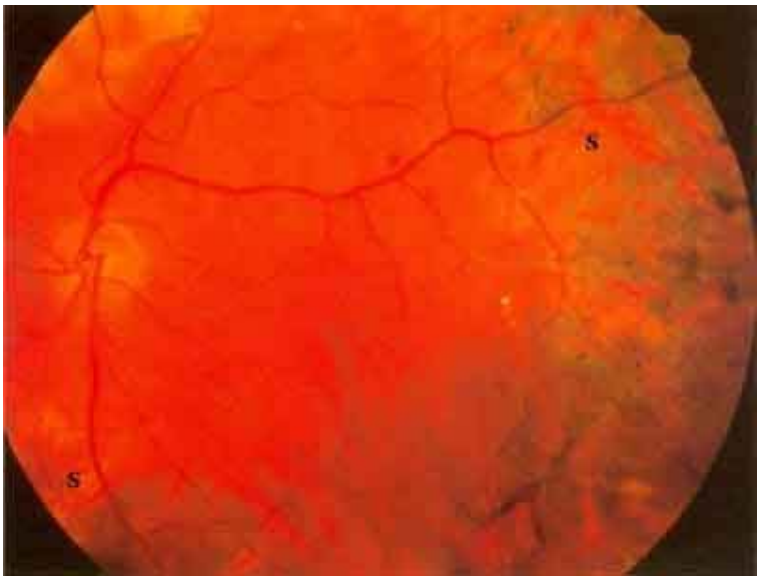

Figure.12 HIGH-RISK PROLIFERATIVE DIABETIC RETINOPATHY POST TREATMENT WITH PAN-RETINAL LASER PHOTOCOAGULATION SCARS (s) TEMPORARILY AND NASALLY -- DISC NEW VESSELS REGRESSED

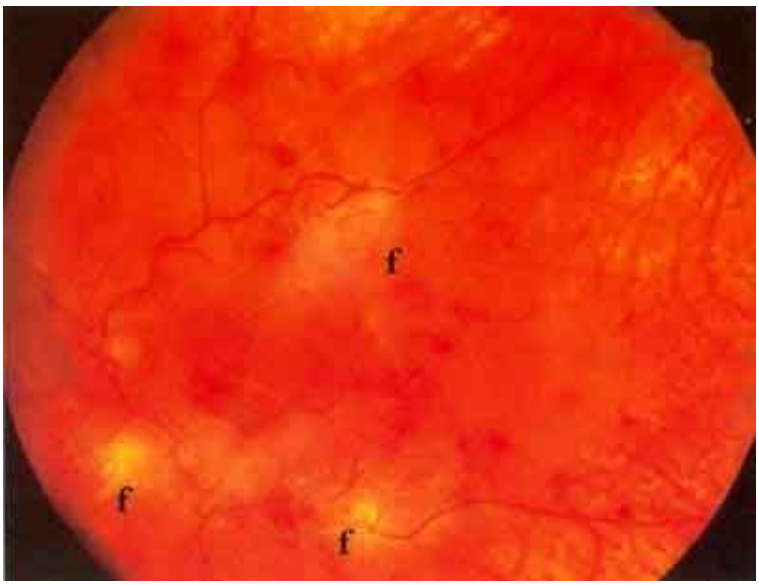

Figure.13 ADVANCED PROLIFERATIVE DIABETIC RETINOPATHY PRERETINAL FIBROVASCULAR TISSUE PRODUCING TRACTION ON RETINA (f) ACROSS THE MACULAR REGION

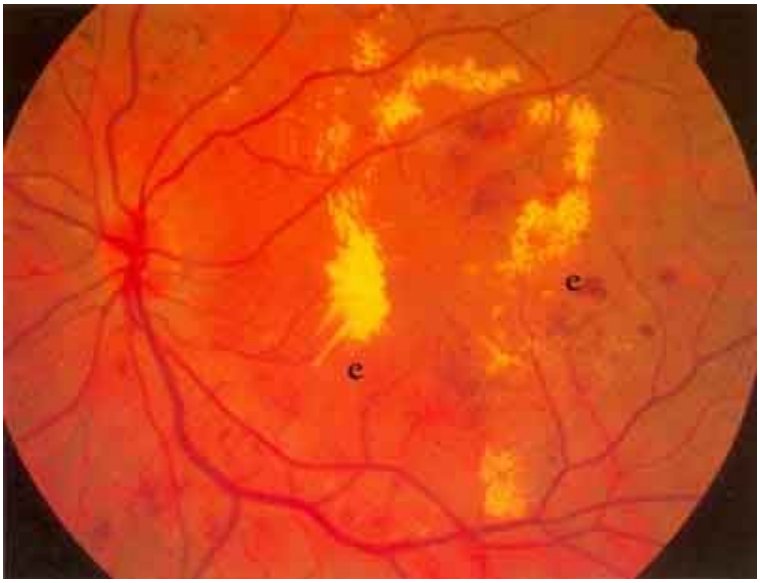

Figure.14 CLINICALLY SIGNIFICANT MACULAR OEDEMA LOCALIZED AREA OF RETINAL OEDEMA SURROUNDED BY LIPID EXUDATES (E) EXTENDING TO THE MACULA

Estimation of GFR

The GFR per 1.73 m^2 BSA was calculated with serum creatinine, urea nitrogen, and albumin levels using an equation developed from the Modification of Diet in Renal Disease (MDRD) Study, as follows:

$$\mathbf{GFR = 170 \times [serum\ creatinine]^{-0.999} \times [age]^{-0.176} \times [0.762\ if\ female] \times [1.180\ if\ non\ Hispanic\ black] \times [blood\ urea\ nitrogen]^{-0.170} \times [serum\ albumin]^{-0.318}}$$

The MDRD GFR calculator was available from internet at the following address http://www.nephron.com/MDRD_GFR.cgi and was utilized to calculate GFR.

Selection and Details of Study subjects

Out of 406 diabetic individual evaluated during the study period 73 were excluded due to elevated sr.creatinine, 75 had macro proteinuria, 57 was diagnosed to have micro albuminuria and 25 were eliminated since they were on ACEI / ARBS. Leaving 186 patients for study .Type 1 DM comprised 25 patients and 161 came under Type 2 DM category respectively. Data were collected in a cross-sectional way during their hospital stay . Patients were initially screened with early morning urine for spot protein creatinine ratio and then based on absence of macro proteinuria 24 hrs urinary protein was done to assess the presence of any significant proteinuria..The test was repeated 3 times and average of three was taken as absence of significant proteinuria. Optic fundus was studied with ophthalmosope and assessed for retinopathy. Blood pressure was measured with mercury manometer and average of 6 BP recordings were taken for analysis. Sr. creatinine and blood glucose were analysed using ERB 300 full auto analyzer.

Haemoglobin was estimated using coulter counter. Urine protein was analysed using auto analyzer. Data was analysed with MINITAB 15 statistical software .cross tabulation and chi square analysis was done using the variables recorded.

Inclusion criteria

TYPE 1 DM AND TYPE 2DM

1.40 years of age or older and completed a standardized interview and a detailed physical examination and classified as having type 2 DM according to the American Diabetes Association (ADA)

2. Type 1 with a duration of at least 10 years

3. Normoalbuminuria

4. serum creatinine <2.0 mg/dl

5. Absence of clinical evidence of other glomerulopathies.

Exclusion criteria

Patients known to be microalbuminuric before antihypertensive therapy was started were not eligible for this study and those who were on ACEI / ARBS were excluded.

Patients with urinary tract infection, congestive heart failure , acute severe elevations of blood pressure or blood glucose or menstruation urine samples were taken after the patients had recovered from the acute illness.

Symptoms interviewed for :

Polyuria, polydipsia, polypaghia

Weight loss

Chest pain ,palpitation, breathlessness,

Swelling of lower limbs, facial puffiness,

Dysuria, oliguria, hematuria,

Pruritis vulva,

Pins and needles burning sensation in extremities

Foot infection, amputation, diabetic foot,

Diminison of vision

Acute complications (DKA, hypoglycemia, hyperosmolar state, cereberovascular accidents, myocardial infarction, unstable angina,Non-STEMI,)

Absent sweating,postural giddiness, chronic diarrhea or constipation.

History of cardiovascular events (e.g, myocardial infarction, other acute coronary syndromes),hypertension, peripheral vascular disease, retinopathy, smoking, alcohol consumption, intake ACEI medication.

EXAMINATION:

Height, weight., waist circumference,

Pulse,peripheral pulses,

Blood pressure (mean of 6 readings) ,postural drop of BP.

DEFINATION

	Systolic	diastolic
High normal	130--139	90—99
Hypertension		
Stage I (mild)	140—159	90—99
Stage II (moderate)	160—179	100—109
Stage III (Severe)	>180	> 110

Isolated systolic hypertension	>140	<90

RETINOPATHY

I .Normal fundus

II. Background retinopathy

III. Proliferative retinopathy

Investigation

Blood Hb in gm%:

Urine for sugar , albumin, deposit,

Blood glucose, blood urea, sr, creatinine

Lipid profile

Urine spot protein creatinine ratio,

24 hrs urinary protein (average of three samples)

I .More than 300mg/24 hrs – proteinuria

RESULTS:

Out of 186 patients 161 were categorized to Type2 DM and 25 to Type 1 DM. Among males 14(13%) were type 1 DM and 97 (87%) were type 2 DM . 11 (14%) females fell under the category of type 1 DM and 64 (86%) in type 2 DM (table 1).

S.NO	TYPE OF DIABETES MELLITUS	MALE		FEMALE	
		NO.	%	NO.	%
1.	TYPE 1	14	12.61	11	14.67
2.	TYPE 2	97	87.39	64	85.33
	TOTAL	111	100	75	100

TABLE 1 .TYPE OF DIABETES MELLITUS AND SEX DISTRIBUTION

	TYPE 1DM GFR in ml/min			TYPE 2DM GFR in ml/min		
	>90	60-89	30-59	>90	60-89	30-59
MALE	5	2	7	20	19	58
FEMALE	5	1	5	8	18	38
TOTAL	10	3	12	28	37	96

TABLE 2

SEX DISTRIBUTION ACCORDING TO GFR IN TYPE 1 DM AND TYPE 2 DM

The mean age was 53 ± 13 years among the total study group and the mean duration of illness was 6 ± 7years. 15 patients under type 1 DM and 133 patients under type 2 DM had GFR < 90ml/min.(table 2)

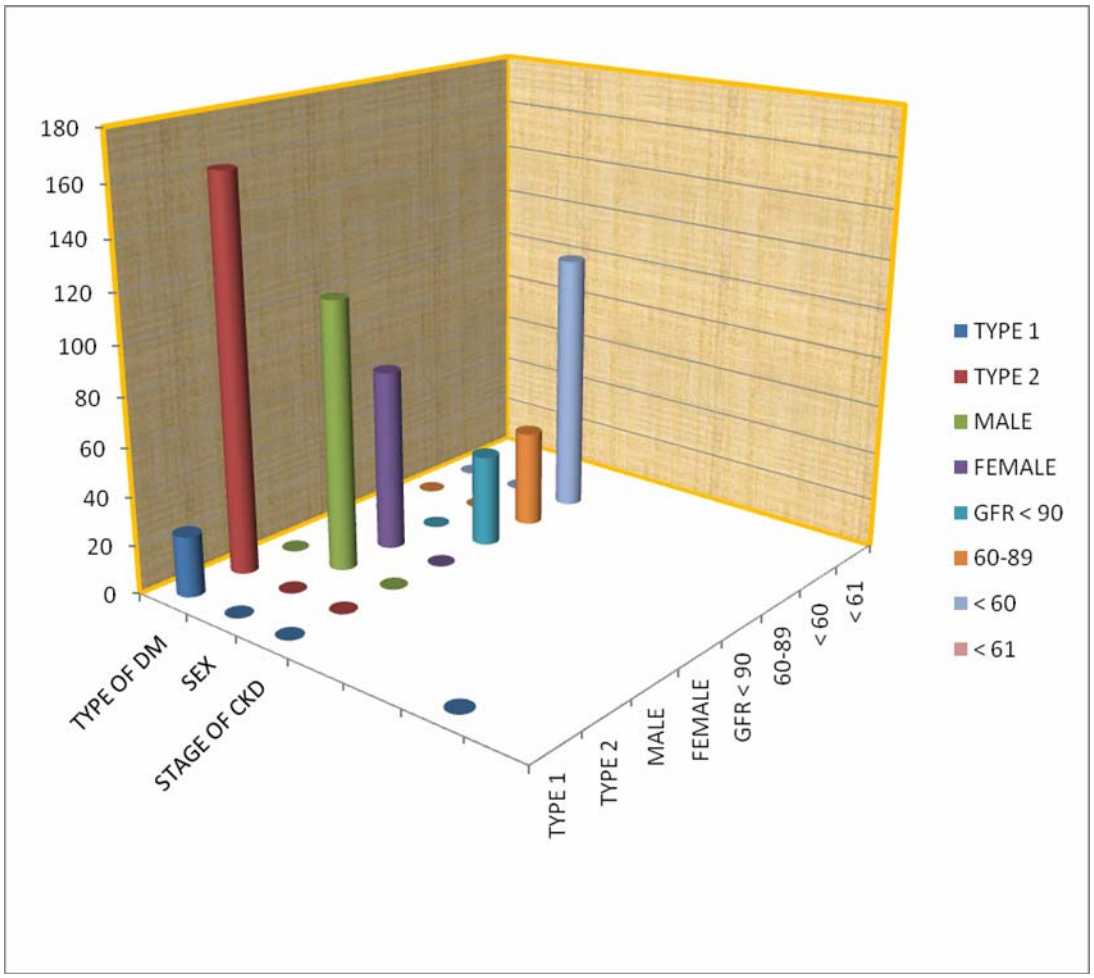

Figure: 15 Graph depicting the distribution of type of diabetes , sex and stages of chronic kidney disease

TABLE 3 . DURATION OF DIABETES IN BOTH TYPES OF DIABETES

DURATION OF ILLNESS	TYPE 1 DM		TYPE 2 DM	
	No.	%	No	%
Recently Diagnosed	-	-	66	41.250
1—5 yrs	-	-	37	23.125
6—10yrs	-	-	32	20
11—15yrs	16	64	16	10
16—20yrs	4	16	7	3.75
20---25yrs	2	8	1	0.625
25—30yrs	2	8	1	0.625
30—35yrs	1	4	1	0.625
TOTAL	25	100	161	100

DM- DIABETES MELLITUS

Among Type 1 DM 14 (64%) patients had duration of diabetes for 11—15 years with mean duration of illness 15 (± 6)years with maximum of 35 years.(table .2)

In type 2 DM 66(41.2 %) patients was recently diagnosed with mean duration of 5 (± 6) years and maximum of 34 years.(table.3)

TABLE 4 . DIABETES AND CARDIOVASCULAR MORBIDITY

	SYMPTOMS	TYPE 1DM			TYPE 2 DM		
1	Cardiovascular Symptoms	M	3	6.9%	M	40	93.1%
		F	3	11.1%	F	27	88.9%
2.	History of Hypertension	M	0	0%	M	28	52.8%
		F	0	0%	F	25	47.2%
3	History CAD/ MI	M	0	0%	M	32	72.7%
		F	0	0%	F	12	27.3%

CAD- CORONARY ARTERY DISEASE

MI- MYOCARDIAL INFARCTION

93% of males in type 2 DM had cardiovascular symptoms, while only 6.9% of type 2 DM patients had similar symptoms. 88.9% of females under type 2 DM and 11% in type 1 DM category had clinical symptoms pertaining to cardiovascular illness.(table .3) 52% of males and 47% of females in type 2 DM group had revealed as they were suffering from hypertension. None of type 1 DM patients gave history of hypertension ref: table .3.

72% of males and 27% of females in type 2 DM had acute coronary events either in the form of myocardial infarction or unstable angina. There were no similar events recorded under type 1 DM category. (table.4)

TABLE.5 TYPE OF DIABETES, SEX, CAD/MI IN RELATION TO GFR

	TYPE 1 DM CAD/ MI IN RELATION TO GFR			TYPE 2 DM CAD /MI IN RELATION TO GFR		
	>90	60-89	30-59	>90	60-89	30-59
MALE	0	0	0	10	3	19
FEMALE	5	2	7	10	18	39
TOTAL	5	2	7	20	21	58

CAD- CORONARY ARTERY DISEASE

MI- MYOCARDIAL INFARCTION

9 patients in type 1 DM and 79 patients in type 2 DM had GFR less than 90 ml/min.

7 patients in type 1 DM and 58 patients in type 2DM had GFR <60 ml/min.(table 5)

TABLE 6. DIABETIC PERIHERAL NEUROPATHY AND DIABETIC FOOT

	SYMPTOMS	TYPE 1 DM			TYPE 2 DM		
1	Symptoms of diabetic neuropathy	M	3	50%	M	25	65.8%
		F	3	50%	F	13	34.2%
2.	Peripheral vascular disease	M	0	0%	M	20	77%
		F	0	0%	F	6	23%
3	History of non healing foot ulcers	M	0	0%	M	18	78.2%
		F	0	0%	F	5	21.8%

DM-DIABETE MELLITUS

65% of type 2 DM males and 50% of type 1 DM males had symptoms of sensory disturbances over distal extremites while 50% of type 1 DM females and 34% of females diseased with type 2 DM had similar symptoms.

77% of type 2 DM males and 23% of type 2 DM females had peripheral vascular disease in the form of feeble or absent peripheral pulses. None of the type 1 DM patients suffered from similar complaints.

78% of type 2 DM males and 22% of type 2 DM females had longstanding non healing foot ulcers.. None of type 1 DM individuals had similar situation. (table 6)

TABLE 7. ACUTE COMPLICATIONS OF DIABETIC PATIENTS IN STUDY POPULATION

S.NO	COMPLICATIONS	TYPE1 DM		TYPE 2 DM		CUMULATIVE			
		total	%	total	%	M	F	total	%
1.	Diabetic ketoacidosis	2	8	10	6.2	7	5	12	6.45
2.	Hypoglycemia	1	4	7	4.3	5	3	8	4.3
3.	Cereberovascular Accident	0	0	10	6.2	7	3	10	5.38
4.	Myocardial infarction	0	0	9	5.6	7	2	9	4.84
5.	Non-STEMI / Unstable angina	0	0	7	4.3	1	6	7	3.76
6.	Hyperosmolar coma	0	0	2	1.2	1	1	2	1.07
	total	3	12	45	27.9	28	20	48	25.8

Non-STEMI-non ST elevation myocardial infarction

The prevalence of acute complication among type 1 DM was 12% and 27.9% in type 2 DM .Diabetic ketoacidosis occurred in 6.45% in both groups. 4.3% had hypoglycemia and 5.38% of patients had cereberovascular accidents. Myocardial infarction was the presenting complication in 4.84% of both categories. Acute coronary syndrome in the form of unstable angina and Non- STEMI happened in 3.76% of patients. Overall complications in both groups was 25.8%. Males encountered 15.05% and females had 10.75% complications. (table. 7).(figure ;16)

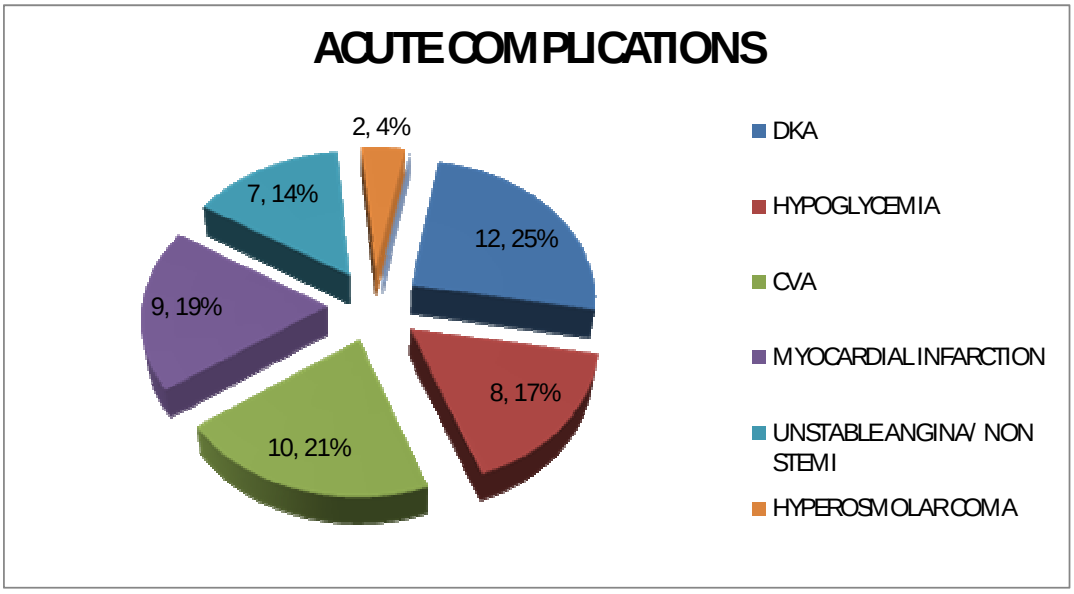

Figure 16: Graph depicting the distribution of acute complications encountered by study population

TABLE 8 RETINOPATHY IN THE DIABETIC PATIENTS IN STUDY GROUP

S.NO	COMPLICATIONS	TYPE1 DM		TYPE2 DM		CUMULATIVE			
		total	%	total	%	M	F	total	%
1.	CATRACT	0	0	55	34.2	29	26	55	29.6
2.	NORMAL FUNDUS	19	76	61	37.9	53	27	80	43
3.	BACKGROUND RETINOPATHY	6	24	34	21.1	22	18	40	21.5
4.	PROLIFERATIVE RETINOPATHY	0	0	11	6.8	7	4	11	5.9
5.	TOTAL RETINOPATHY	6	24	45	27.9	29	22	51	27.4

DM-- DIABETES MELLITUS

Fundus examination revealed only 24% background retinopathy and no findings suggestive of proliferative retinopathy in type 1 DM . Among type 2 DM 21.1% had background retinopathy and 6.8% had proliferative retinopathy. Retinal study could not be done in 29.6% due to mature cataract. While comparing sex preponderance males had 15.59% and females 11.82% accounting for a total 27.4% of diabetic retinopathy in both the groups of study population.(table 8)

TABLE 9. RELATION OF TYPE OF DIABETES, SEX, RETINOPATHY TO GFR

		TYPE 1DM RETINOPATHY IN RELATION TO GFR			TYPE 2DM RETINOPATHY IN RELATION TO GFR		
		>90	60-89	30-59	>90	60-89	30-59
MALE	BR	0	0	2	0	2	18
	PR	0	0	4	0	1	13
FEMALE	BR	0	0	0	0	1	6
	PR	0	0	0	1	1	2

BR-BACK GROUND RETINOPATHY

PR- PROLIFERATIVE RETINOPATHY

39 patients with type2 DM had retinopathy whose GFR were less than 60ml/min while only 6 patients with type 1 DM patients with retinopathy had GFR < 60 ml/min.(table 9)

TABLE 10 GRADING OF BLOOD PRESSURE IN STUDY GROUP

	BLOOD PRESSURE	MALE		FEMALE		TYPE 1 DM		TYPE2 DM	
		NO.	%	NO	%	NO	%	NO	%
1.	Normal BP	13	11.7	16	21.3	5	20	24	14.9
2.	130-139 / 85-89	26	23.4	16	34.6	7	28	45	27.9
3.	140-150 / 90-99	34	30.6	27	36	12	48	49	30.4
4.	160-179 /100-109	16	14.4	1	1.3	1	4	16	9.9
5.	>180 / >110	5	4.5	2	2.7	0	0	7	4.3
6.	>140 / < 90 Isolated systolic hypertension	17	15.3	3	4	0	0	20	12.4
7.	Total Hypertensive patients	72	64.8	33	44	13	52	92	57.1

The prevalence of hypertension in the study population was 56.4%, in which males contributed 38.7% and females about 17.7% combining both groups. In both the groups more than 50% had hypertension and most of fell under the category of stage 1.

15% of males and 4% of females had isolated systolic hypertension(table 10)

TABLE.11 GFR OF STUDY GROUP WITH REFERENCE TO STAGES OF CHRONIC KIDNEY DISEASE

S.NO	GFR ml/min	TYPE 1 DM				TYPE 2 DM			
		NO.		%		NO.		%	
		M	F	M	F	M	F	M	F
1.	> 90	5	5	20	20	20	8	12.4	4.9
2.	60—89	2	1	8	4	19	18	11.8	11.1
3.	30--59	7	5	28	20	58	38	36	23.6
4.	15--29	--	--	--	---	---	---	---	---
5.	< 15	---	---	---	---	---	---	---	---

GFR- GLOMERULAR FILTERATION RATE

MDRD- MODIFIED DIET AND RENAL DISEASE

DM- DIABETES MELLITUS

. In our study under type 1 DM category 12% under stage 2 CKD comprised 8 % of males and 4% of females .Out of 48% under stage 3 of CKD 28% were males and 20% were females respectively in absence of microalbuminuria.

Similarly under type 2 DM category 22.9% under stage 2 CKD comprised 11.8 % of males and 11.1% of females .Out of 59.6% under stage 3 of CKD 36% were males and 23.6% were females respectively in absence of microalbuminuria(table 11)

TABLE 12. BLOOD PREEURE AND ITS RELATION TO RETINOPATHY AND GFR

	BLOOD PRESSURE	RETINOPATHY				GFR BY MDRD					
		BR		PR		>90		60--89		30--59	
		No	%	No	%	No	%	No	%	No	%
1.	Normal BP	8	15.7	3	5.9	6	15.7	8	20	15	13.8
2.	130-139 / 85-89	9	17.6	3	5.9	13	34.2	13	32.5	26	24
3.	140-150 / 90-99	16	31.3	5	9.8	9	23.6	10	25	42	38.8
4.	160-179 /100-109	1	1.9	0	0	2	5.26	7	17.5	8	7.4
5.	>180 / >110	2	3.9	0	0	0	0	0	0	7	6.4
6.	>140 / < 90 Isolated systolic hypertension	4	7.8	0	0	8	21	2	5	10	9.26
7.	Cumulative Percentage in category	40	78.4	11	21.6	38	20.4	40	21.5	108	58

BR- BACKGROUND RETINOPATHY

PR- PROLIFERATIVE RETINOPATHY

GFR- GLOMERULAR FILTERATION RATE

MDRD- MODIFIED DIET AND RENAL DISEASE

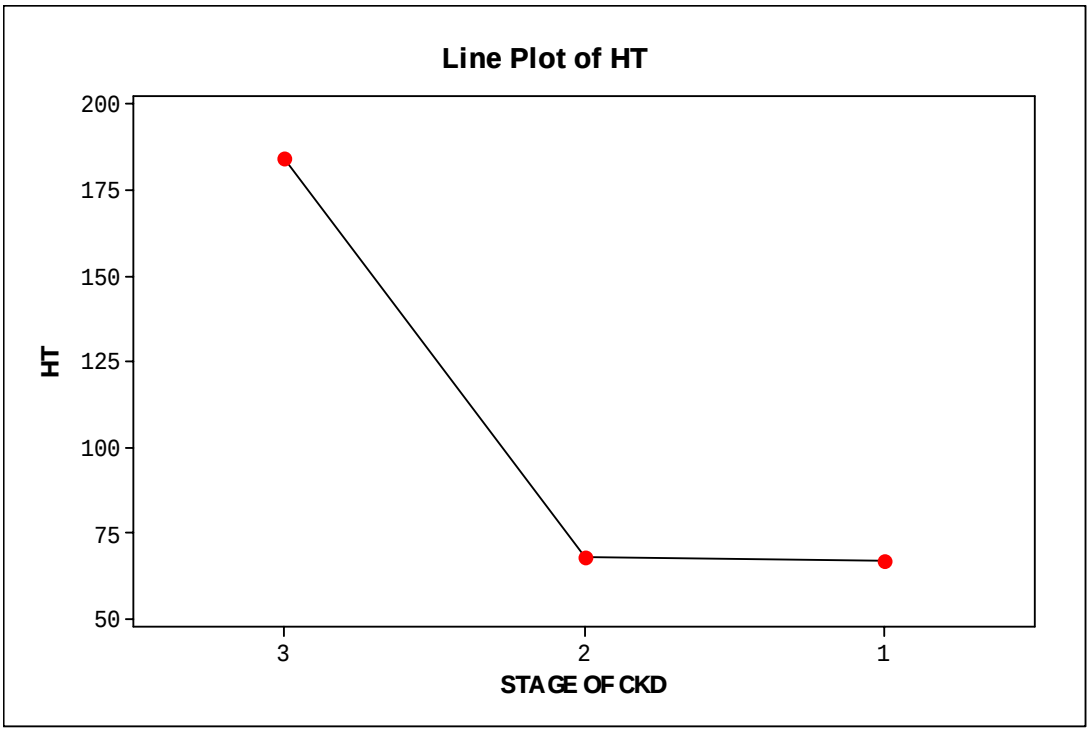

FIGURE- 17 RELATIONSHIP OF HYPERTENSION TO STAGE OF CHRONIC KIDNEY DISEASE

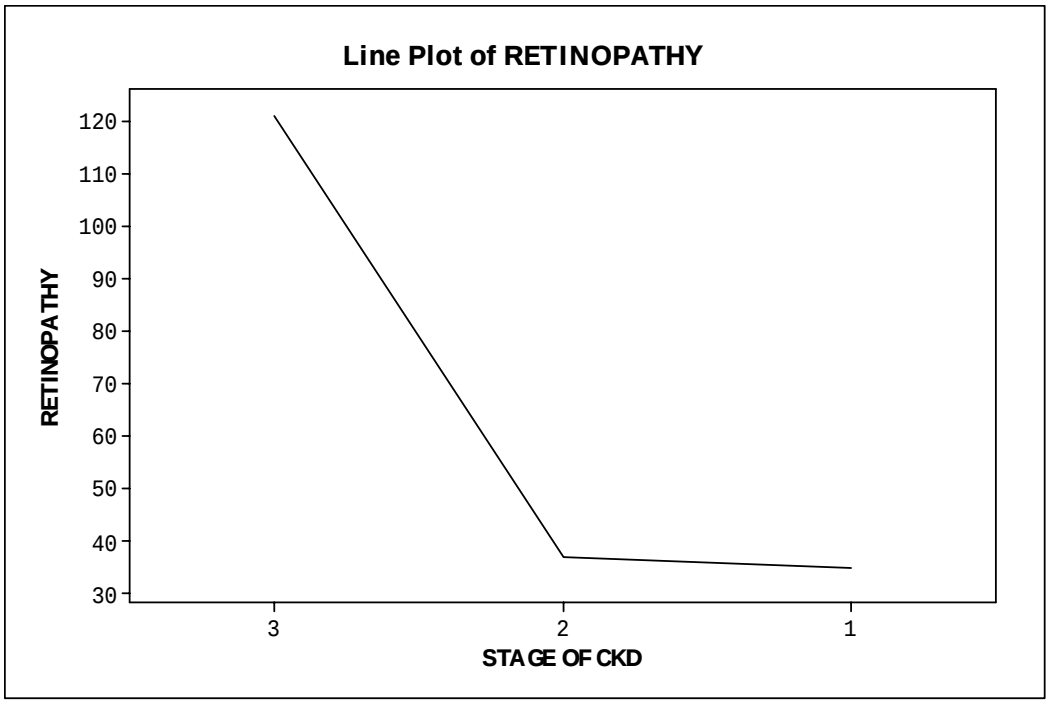

FIGURE 18 –RELATIONSHIP OF RETINOPATHY TO STAGE OF CHRONIC KIDNEY DISEASE

The relation between blood pressure to GFR and retinopathy was analysed . Of total 51 patients who had retinopathy 78.4% had background retinopathy and 21.6% patients had proliferative retinopathy . 17.6 % of patients with background retinopathy 5.9% patients fell under the category of stage 1 hypertension . 31.3% of patients with background retinopathy and 9.8% patients with proliferative retinopathy were in stage 2 category of hypertension. . less than 4% with retinopathy were in stage 3 and 4 of hypertension. There was a significant correlation when analysed with pearson's statistical correlation method. (p value = 0.159).(table 18)

32.5% under CKD stage 2 and 24% of stage 3 CKD was under stage 1 hypertension. and 25 and 38.8 percent patients in stage 2 and stage 3CKD came under stage 2 hypertension . 17.5 and 7.4 percent of patients in satge 2 and stage 3 CKD fell under stage 3 hypertension.(table 18)

The relation of GFR calculated by MDRD formula and blood pressure was analysed using the same statistical method and significant correlation was found.

DISCUSSION AND COMPARATIVE ANALYSIS:

Long-standing type 1 diabetic patients with normal albumin excretion rate are still at risk of developing clinically significant nephropathy . It is therefore important to identify markers of increased nephropathy risk among these patients. One possibility is to perform kidney biopsies in such patients, given that those with more advanced glomerulopathy are more likely to develop abnormalities in albumin excretion rate . However, this is not very practical in most clinical settings. So the study was conducted whether reduced GFR can be predictive of more advanced underlying glomerular lesions. In the present study out of 406 patients which included both type1 DM and type 2 DM 18% had macro-albuminuria and 14% had microalbuminuria and 45% had normo albuminuria.

Among normoalbuminuria under type 1 DM category 12% under stage 2 CKD (GFR -60-89ml/min) comprised 8 % of males and 4% of females .Out of 48% under stage 3 of CKD (GFR- 30—59ml/min) 28% were males and 20% were females respectively in absence of albuminuria.

Similarly under type 2 DM category 22.9% under stage 2 CKD (GFR -60-89ml/min) comprised 11.8 % of males and 11.1% of females .Out of 59.6% under stage 3 of CKD (GFR- 30—59ml/min) 36% were males and 23.6% were females respectively in absence of albuminuria

.In the third NHANES survey, Kramer *et al.* total of 1180 adults with previously diagnosed type 2 DM were included in the study Among the adults with previously diagnosed type 2 DM, the mean reported duration of DM was 9.1 years, and 25% and 51% reported the use of insulin and diabetes pills, respectively.

In the present study 23% were recently diagnosed and 20% and 10% with the duration of

illness for 6-10 years and 11-15 years in type 2 DM category.. Only 64.2% (n=45) of type 2 DM were on regular treatment. All type 1 DM were on regular insulin treatment.

Albuminuria (spot urine albumin/creatinine ratio) were absent in 30% of elderly type 2 diabetic patients with GFR <60 ml/min per 1.73 m^2 (Modification of Diet in Renal Disease [MDRD] formula) . Adults with type 2 DM and CKD were more likely to have macroalbuminuria (19%), microalbuminuria (45%), and diabetic retinopathy (28%).

In the present study which included both type1 DM and type 2 DM 18% had macro-albuminuria and 14% had microalbuminuria and 45% had normo albuminuria.

Among all adults with type 2 DM (previously diagnosed and newly diagnosed by ADA criteria) with macroalbuminuria (population estimate, 0.5 million), 31% (n = 56) had diabetic retinopathy (population estimate, 0.2 million). Among individuals with microalbuminuria (population estimate, 3.0 million), 21% (n = 107; population estimate, 0.6 million) had diabetic retinopathy. Thirteen percent (n = 84; population estimate, 0.6 million) with diabetic retinopathy did not have microalbuminuria or macroalbuminuria.

In the present study 27.4% (n=51) with diabetic retinopathy did not have microalbuminuria or macroalbuminuria

Study conducted by M. Luiza Caramori, Paola Fioretto, and Michael Mauer in

105 patients (65 women) were studied. Age was 35.4 ± 9.1 years, age at diabetes onset 12.6 ± 7.2 years, and diabetes duration 22.7 ± 9.3 years.

In the present study the duration of illness was more than 10 years in type 1 DM . under type 2 DM 23% were recently diagnosed and 20% and 10% with the duration of illness for 6-10 years and 11-15 years. 75 patients were women as opposed to 111 men.

Retinopathy was present in 67 patients (64%); 25 (24%) had proliferative changes.

In the present study out total 51 patients who had retinopathy 78.4% had background retinopathy and 21.6% patients had proliferative retinopathy.

Hypertension was present in 38 (36%) patients; Altogether, 23 (22%) patients were in the low and 82 (78%) patients were in the normal GFR groups. There were more women in the low GFR than in the normal GFR group . The prevalence of hypertension was the same in both groups ; however, when defined as blood pressure values ≥140/90 mmHg or use of antihypertensive drugs, the prevalence was greater in the low GFR group .

The prevalence of hypertension in the present study was 56.4%, in which males contributed 38.7% and females about 17.7% combining both groups. In both the groups more than 50% had hypertension and most of fell under the category of stage 1 hypertension. 39 % (n=74) of hypertensive patients were in low GFR group while 10% (n=19) hypertensives were in normal GFR group.

15% of males and 4% of females had isolated systolic hypertension

The prevalence of any retinopathy was more frequent in low versus normal GFR patients , as was proliferative retinopathy .(ref :32)

In the present study out total 51 patients who had retinopathy 78.4% had background retinopathy and 21.6% patients had proliferative retinopathy and retinopathy was more frequent in low GFR (GFR= < 90 ml/min) group(26.8%).

PH Lane, MW Steffes and SM Mauer and colleagues reported eight women with type 1 DM with low creatinine clearance rate (CCR) and normal urinary albumin excretion. (ref: 27)

In the present study (n=15/25) 60%of type 1 DM had low GFR. Females contributed 24% with low GFR.

Caroline K. Kramer and colleagues in their study reported out of total 660 normoalbuminuric type 2 diabetic patients were evaluated, Eighty-four (12.7%) had low GFR (15–60 ml/min per 1.73 m^2), and the remaining 576 comprised the reference group (87.2%) .The group of patients with low GFR was older (62.9 ± 10.3 vs. 56.8 ± 9.5 years), had more women (77.4 vs. 60.2%).

In the present study of 406 patients which included both type1 DM and type 2 DM 45% had normo albuminuria. 60% under type 1 DM and 82.5% under type 2 DM

had CKD (GFR < 90 ml/min). 58% under stage 3 (GFR= 30—59ml/min). Regarding

sex involvement males out numbered females { 46% (n=86) vs 33% (n=46.2) }. CKD also occurred more frequently after 60 years { 55.3% (n=103) }

The prevalence of micro- and macrovascular diabetes complications in low GFR group was (diabetic retinopathy: 28.4% $P = 0.037$; coronary heart disease: 29.2% $P = 0.729$; peripheral vascular disease: 33.3 %, $P = 0.089$; and cerebrovascular disease: 7.7% $P = 0.218$) (ref: 29)

. In the present study diabetic complication in low GFR group was(diabetic retinopathy: 26.8% $P = 0.575$; coronary heart disease: 17.2% $P = 0.331$; peripheral vascular disease: 12.3 %, $P = 0.331$; and cerebrovascular disease: 4.8% $P = 0.019$)

Study conducted by Richard J. MacIsaac and colleagues revealed in about 109 patients (36%) had a GFR <60 ml · min^{-1} · 1.73 m^{-2}. The overall prevalence of normo-, micro-, and macroalbuminuria was 43 of 109 (39%), 38 of 109 (35%), and 28 of 109 (26%), respectively. Compared with patients with macroalbuminuria, those with normoalbuminuria were more likely to be older and female.

In the present study out of 406 patients which included both type1 DM and type 2 DM

18% had macro-albuminuria and 14% had microalbuminuria and 45% had normo albuminuria.

Males were predominatly affected than females . Older individuals were commonly affected as seen in Richard J. MacIsaac and colleagues study. (ref:28)

In several independent local surveys it was found that 15 to 20% of type 2 diabetic patients reaching end-stage renal failure lacked major proteinuria and had shrunken kidneys, raising the unproven assumption of ischemic nephropathy.

Vincent Rigalleau et al in their study of 89 patients with diabetes and a modification of diet in renal disease (MDRD) estimated GFR (e-GFR) <60 ml/min per 1.73 m^2 underwent a 51Cr-EDTA B-isotopic GFR determination and were followed up for 38 ± 11 months.

The mean MDRD e-GFR (41.3 ± 13.1 ml/min per 1.73 m^2) did not significantly differ from the i-GFR (45.6 ± 29.7). Of the subjects, 15 (17%) were normoalbuminuric. Their i-GFR did not differ from the albuminuric rate and from their MDRD e-GFR, although their serum creatinine was lower (122 ± 27 vs. 160 ± 71 μmol/l, $P < 0.05$): 71% would not have been detected by measuring serum creatinine (sCr) alone. They were less affected by diabetic retinopathy.($P < 0.05$ vs. albuminuric).(ref:31)

In the present study out of 406 patients which included both type1 DM and type 2 DM 18% had macro-albuminuria and 14% had microalbuminuria and 45% had normo albuminuria. In the present study out total 51 patients who had retinopathy 78.4% had background retinopathy and 21.6% patients had proliferative retinopathy in the absence of albuminuria.

SUMMARY:

From the study ANALYSIS OF GFR IN NON-ALBUMINURIC TYPE-1 AND TYPE-2 DIABETES MELLITUS IN EARLY DETECTION OF CHRONIC KIDNEY DISEASE - CROSS-SECTIONAL STUDY conducted in Govt. Madurai Rajaji Hospital in Department of Medicine and Department of diabetology in186 patients , it was found that both type 1(n=15/25) and type 2 (n=133/161) diabetic patients had nephropathy in the absence of significant urinary albumin.

1. Out of 186 patients 161 were categorized to Type2 DM and 25 to Type 1 DM. Among male 14(13%) were type 1 DM and 97 (87%) were type 2 DM . 11 (14%) females fall under the category of type 1 DM and 64 (86%) in type 2 DM.
2. Among Type 1 DM 14 (64%) patients had duration of diabetes for 11—15 years. In type 2 DM 66(41.2 %) patients was recently diagnosed.
3. Among normoalbuminuria under type 1 DM category 12% under stage 2 CKD (GFR -60-89ml/min) comprised 8 % of males and 4% of females .Out of 48% under stage 3 of CKD (GFR- 30—59ml/min) 28% were males and 20% were

females respectively in absence of albuminuria.

Similarly under type 2 DM category 22.9% under stage 2 CKD (GFR -60-89ml/min) comprised 11.8 % of males and 11.1% of females .Out of 59.6% under stage 3 of CKD (GFR- 30—59ml/min) 36% were males and 23.6% were females respectively in absence of albuminuria

4. In the present study which included both type1 DM and type 2 DM 18% had macro-albuminuria and 14% had microalbuminuria and 45% had normo albuminuria.
5. In the present study out total 51 patients who had retinopathy 78.4% had background retinopathy and 21.6% patients had proliferative retinopathy in the absence of albuminuria.
6. The prevalence of hypertension in the present study was 56.4%, in which males contributed 38.7% and females about 17.7% combining both groups. 39 % (n=74) of hypertensive patients were in low GFR group while 10% (n=19) hypertensives were in normal GFR group.

7. . In the present study diabetic complication in low GFR group was(diabetic retinopathy: 26.8% $P = 0.575$; coronary heart disease: 17.2% $P = 0.331$; peripheral vascular disease: 12.3 %, $P = 0.331$; and cerebrovascular disease: 4.8% $P = 0.019$)

Alternatively the kidney may be the victim of extrarenal factors such as a history of hypertension, malnutrition, or cholesterol microembolism, to mention only a few. It will be particularly relevant to address the above potential non classical pathogenetic pathways if it were ever to arrive at specific targeted interventions for this segment of the diabetes population. Lurbe et al. (ref:25) recently reported that nighttime ambulatory blood pressure values and “nondipper” status were significant predictors of

progression from normoalbuminuria to microalbuminuria in adolescent patients with type 1 diabetes. Unfortunately night time ambulatory blood pressure monitoring was not possible due non availability of measuring device,.but a 6 times blood pressure recording was done to minimize the errors

Parving et al stated that the absence of retinopathy greatly reduced the likelihood that albuminuria was due to diabetic glomerulosclerosis in type 1 or type 2 DM. In the absence of retinopathy or albuminuria in 30% of adults with a GFR less than 60 mL/min per 1.73 m^2 BSA, classic diabetic glomerulosclerosis is unlikely to be the underlying renal pathology

CONCLUSION:

In conclusion, more than 50% adults 40 years of age or older with type 2 DM and patient with type 1 DM for more than period of 10 years had CKD either in stage 1 or stage 2.

36%(n=9/25) of males and 24%(n=6/25) of females had low GFR (GFR=< 90 ml/min) under type 1 DM. Similarly in type 2 DM(n=77/161) 47.8% males and (n=56/161) 34.7% females had decreased GFR in absence of albuminuria.

25% with CKD were less than 50years and 55.3% were more than 50years old.

16% of females and 8% males with retinopathy had low GFR in type 1 DM group.. While 16.7% males and 11.1% females with retinopathy had low GFR in type 2 DM group.

1.. The results suggest that serum creatinine levels should be measured and GFR to be estimated in all diabetic individuals who are at risk of developing nephropathy in

addition to monitoring urine albumin excretion and funduscopic changes to screen for kidney disease.

2. Because it would not be practical to perform renal biopsies in all normoalbuminuric patients, it is recommended that long-standing normoalbuminuric diabetic patients with retinopathy or hypertension should have GFR measured on a regular basis.

3. Since the night time ambulatory blood pressure values and "nondipper" status were significant predictors of progression from normoalbuminuria to microalbuminuria in diabetic patients night time monitoring of blood pressure should be done in those who are at risk of developing diabetic nephropathy

4.The mean MDRD estimated GFR did not significantly differ from the isotope estimated-GFR . So GFR estimation can be safely relayed with MDRD formula.

(ref:31)

LIMITATION OF STUDY

1. The results were predominantly obtained from a cross-sectional survey of patients
2. The sample size in type 1 DM category was small.
3. Night time ambulatory blood pressure could not be recorded.
4. Retinopathy could not be assessed in significant number of patients since they had cataract.
5. Patients recruited here may not be representative of the entire population.
6. Renal biopsy was not done which might have strengthened findings of the study.
7. GFR estimation with inulin or iodothalamate might have improved validity of GFR estimated with MDRD formula.

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PROFORMA

NAME: AGE: SEX:

ADDRESS: OP/IP NO:

OCCUPATION:

TYPE OF DIABETE MELLITUS TYPE 1 / TYPE 2

DURATION OF DISEASE

TREATMENT DETAILS REGULAR / IRREGULAR /

NEWLY DIAGNOSED / NO TREATMENT

SYMPTOMS:

POLYURIA, POLYDISIA, POLYPHAGIA

WEIGHT LOSS

CHEST PAIN , PALPITATION, BREATHLESSNESS

LOWER LIMB SWELLING, FACIAL PUFFINESS

DYSURIA, OLIGURIA, HEMATURIA

PRURITUS VULVA PINS & NEEDLE , BURNING SENSATION IN EXTREMITES

FOOT INFECTION / H/O AMPUTATION / DIABETIC FOOT

DIMINISION OF VISION

ACUTE COMPLICATIONS IF ANY

ABSENT SWEATING, POSTURAL GIDDINESS, DIARRHEA

PAST HISTORY

CAD

HYPERTENSION

PERIPHERAL VASCULAR DISEASE

SMOKING

ALCOHOL

ACEI MEDICATION

EXAMINATION

HEIGHT(cm) WEIGHT(kg) BMI WAIST CIRCUMFERENCE(cm)

PULSE
PERIPHERAL PULSES

BLOOD PRESSURE
(mean of 6 readings)

POSTURAL DROP OF BP

RETINAL EXAMINATION:
GRADING

1. NORMAL FUNDUS
2. BACKGROUND RETINOPATHY
3. PROLIFERATIVE RETINOPATHY

BLOOD Hb in gm%:

URINE SUGAR: ALBUMIN : DEPOSITS:

BLOOD SUGAR :

BLOOD UREA:

SERUM CREATININE:

LIPID PROFILE : LDL VLDL HDL TGL CHOLESTROL

URINE SPOT PROTEIN CREATININE RATIO

24 HRS URINARY PROTIEN 1st SAMPLE 2nd SAMPLE 3rd SAMPLE

Mgs/day

EQUATION FROM MODIFICATION OF DIET IN RENAL DISEASE STUDY

ESTIMATED GFR (ml/min per 1.73m^2) = 1.86 * (Pcr)^-1.154 * (age) ^-0.203

S.NO	NAME	AGE	SEX	TYPE OF DIABETES	DURATION OF ILLNESS IN YEARS	
1	PONNUKALAI	1	1	2	0	2
2	PANDI	64	1	2	0	2
3	MAYAKKAL	48	2	2	0	2
4	NAGARANI	40	2	2	7	1
5	OTCHAMMAL	55	2	2	0	2
6	RATHINAM	60	1	2	4	0
7	ARUMUGAM	65	2	2	4	1
8	KAMATCHI	58	1	2	0	2
9	RAKKAN	62	1	2	5	0
10	PANDI	46	1	2	0	2
11	GURUSAMY	54	1	2	5	0
12	MALAISAMY	65	1	2	20	0
13	BOOMIRAJA	50	1	2	10	0
14	SAMSUDEEN	52	1	2	0	2
15	MATHIVALAN	55	1	2	0	2
16	CHINNARAJA	40	1	2	0	2
17	KRISHNAMOORTHY	71	1	2	20	0
18	GURUNATHAN	58	1	2	15	0
19	RAMAMOORTHY	63	1	2	10	0
20	SAVIOUR	68	1	2	20	0
21	JAYABAL	37	1	2	0	2
22	ANGUSAMY	75	1	2	25	0
23	SIVAKUMAR	48	1	2	5	0
24	LAKSHMAN	72	1	2	0	2
25	RAASHEETH	53	1	2	0	2
26	SELVARAJ	54	1	2	0	2
27	RAJAMOHAN	49	1	2	3	1
28	KARUPPUSAMY	47	1	2	2	1
29	PITCHAI	60	1	2	5	1
30	RENGAIAH	68	1	2	10	0
31	MARUTHAMUTHUPILLAI	40	1	2	10	0
32	KRISHNAN	64	1	2	12	0
33	AYYANAR	40	1	2	0	2
34	MANI	47	1	2	0	2
35	VARGHESE	50	1	2	3	1
36	MADASAMY	70	1	2	5	1
37	MUTHUKRISHNAN	50	1	2	7	0
38	MURUGANATHANAN	60	1	2	4	1
39	PANDI	68	1	2	7	1
40	PARAMASIVAM	47	1	2	0	2
41	MURUGESAN	56	1	2	3	1
42	SEKAR	60	1	2	0	2
43	ABDUL SALEEM	75	1	2	23	1
44	RAMASAMY THEVAR	85	1	2	34	0
45	SENTHIL	48	1	2	0	2
46	SINGARAM	60	1	2	10	1
47	SAMUEL	80	1	2	13	0
48	NATARAJAN	45	1	2	15	1
49	MEENAKHSHI	55	1	2	7	0

	SUNDARAM					
50	RAJENDERAN	45	1	2	0	2
51	PARAMASIVAM	50	1	2	4	1
52	PALANISAMY	50	1	2	10	0
53	BABU	56	1	2	0	2
54	MUTHAIAH	65	1	2	12	0
55	BATCHA	60	1	2	8	0
56	RAMAKRISHNAN	67	1	2	15	0
57	AJMALKHAN	55	1	2	9	0
58	MAYANDI	72	1	2	5	1
59	RENGASAMY	55	1	2	0	2
60	VEERANAN	70	1	2	13	0
61	VEERAMANI	47	1	2	0	2
62	KAMARDEEN	60	1	2	0	2
63	ABDUL MAJEED	55	1	2	4	1
64	GOPAL MOORTHY	57	1	2	10	0
65	CHINNAIH	50	1	2	3	1
66	KAMARDEEN	60	1	2	6	1
67	RASUTHEVAR	72	1	2	14	0
68	NAGAPPAN	58	1	2	6	0
69	PALANI	55	1	2	0	2
70	ARUMUGAM	40	1	2	0	2
71	PURUSHOTHAMAN	70	1	2	12	0
72	KANNAN	43	1	2	0	2
73	THANGAVELU	69	1	2	20	0
74	SHEIK MOHAMMED	66	1	2	0	0
75	SAMSUDEEN	52	1	2	0	2
76	DHARMARAJ	52	1	2	0	2
77	ANTHONY	67	1	2	8	1
78	AYYASAMY	62	1	2	5	1
79	JALEEM	56	1	2	0	2
80	RAMAR	40	1	2	0	2
81	RAMASAMY	70	1	2	15	0
82	THIRUNAVUKU ARASU	42	1	2	0	2
83	PANDI	60	1	2	5	1
84	THANGARAJAN	65	1	2	12	0
85	MARUTHAMUTHUPILLAI	60	1	2	5	1
86	JAYARAMAM	40	1	2	0	2
87	APAAVU	62	1	2	8	1
88	SEKAR	52	1	2	0	2
89	KRISHNAN	60	1	2	7	1
90	GURUSAMY	68	1	2	12	0
91	JEYARAJ	65	1	2	15	0
92	ULAGANATHAN	48	1	2	0	2
93	SETHUPANDI	55	1	2	0	2
94	MUTHUSELVAM	40	1	2	0	2
95	MARIAPPAN	40	1	2	0	2
96	KILAVAPPAN	65	1	2	14	0
97	KARUPPUSAMY	45	1	2	5	1
98	RAMAKRISHNAN	70	1	2	15	0
99	KARUPPANAN	60	1	2	10	0
100	PANDI	73	1	2	0	2

101	MANI	55	1	2	6	1
102	CHINNAMMAL	55	2	2	0	2
103	SARASWATHI	65	2	2	0	2
104	PITCHAIAMMAL	45	2	2	0	2
105	LOGAMMAL	55	2	2	2	1
106	SUNDARAMMAL	60	2	2	0	1
107	JEGATHAMBAL	62	2	2	0	1
108	MUTHULAKSHMI	65	2	2	0	2
109	PUSPAM	65	2	2	4	1
110	KRISHNAVENI	50	2	2	0	2
111	SUGANTHI	67	2	2	0	2
112	LAKSHMI	40	2	2	0	2
113	MARY	55	2	2	5	1
114	MANONMANI	55	2	2	0	2
115	PALANIAMMAL	50	2	2	0	2
116	KAMATCHI	45	2	2	0	2
117	GOMATHI	61	2	2	8	1
118	ANNAPOORANI	59	2	2	7	0
119	POTTAMMAL	55	2	2	2	1
120	VELAMMAL	52	2	2	0	2
121	RADHA	65	2	2	7	0
122	VANAJA	58	2	2	4	1
123	VEERAMMAL	45	2	2	0	2
124	MUNIAMMAL	70	2	2	0	0
125	CHELLAMMAL	48	2	2	6	0
126	ESAKIAMMAL	65	2	2	8	0
127	REGINA	50	2	2	0	2
128	DHANALAKSHMI	67	2	2	3	1
129	MATHI	60	2	2	2	0
130	RAMUTHAI	65	2	2	5	1
131	RAJALAKSHMI	50	2	2	0	2
132	SUNDARAVALLI	62	2	2	5	1
133	PETCHI	60	2	2	6	0
134	NAGARATHINAM	58	2	2	5	0
135	PANAIAMMAL	65	2	2	0	2
136	KURUVAMMAL	50	2	2	0	2
137	JEYAMANI	48	2	2	0	2
138	MEENAKSHI	60	2	2	6	1
139	VELLAIAMMAL	56	2	2	4	1
140	SUNDARI	55	2	2	0	2
141	MUTHU	42	2	2	0	2
142	SUMITHRA	65	2	2	0	2
143	THANGAVELU	55	2	2	5	1
144	SUNDARI	56	2	2	4	0
145	MALAR	56	2	2	0	2
146	MAHALIHAMMAL	65	2	2	10	0
147	AMIRTHAM	65	2	2	5	1
148	SUNDARI	57	2	2	7	0
149	NATCHAMMAL	60	2	2	13	1
150	MARIA PUSPAM	70	2	2	15	0
151	PACKIAYAM	50	2	2	2	1
152	PALANIAMMAL	48	2	2	7	0

153	IRULAYEE	60	2	2	10	0
154	THANGAM	72	2	2	15	0
155	RATHINA VELU	65	2	2	0	2
156	CHANDRA	55	2	2	0	2
157	SANTHANAM	65	2	2	3	1
158	LOGAMBAL	70	2	2	20	0
159	VELLAIAMMAL	55	2	2	5	0
160	FATIMA MARY	53	2	2	0	2
161	AVUDAIAMMAL	60	2	2	6	1
162	MUTHUPANDI	23	1	1	12	1
163	SATISH BABU	29	1	1	10	1
164	MURUGAN	21	1	1	10	1
165	KALAIPPAN	30	1	1	15	1
166	MURUGESAN	39	1	1	20	1
167	RAMAR	57	1	1	35	1
168	ANTHONY	27	1	1	13	1
169	RAJU	35	1	1	20	1
170	SARAVANAN	34	1	1	22	1
171	ARUMUGAM	32	1	1	16	1
172	RAMANATHAN	32	1	1	15	1
173	MURUGESAN	34	1	1	15	1
174	BALAMURUGAN	28	1	1	12	1
175	PANDIARAJAN	33	1	1	15	1
176	THANGAM	30	2	1	13	1
177	KARUPPANNAN	27	2	1	13	1
178	MAYILVAHANNAN	40	2	1	24	1
179	MALAR VIZIHI	24	2	1	10	1
180	AMEENA BEEVI	22	2	1	10	1
181	DHANALAKSHMI	20	2	1	10	1
182	LAKHSMI	30	2	1	16	1
183	ALAGI	48	2	1	25	1
184	MALAR	25	2	1	10	1
185	JEYASEELA	38	2	1	22	1
186	INDIRANI	28	2	1	10	1

CHEST PAIN PALPITATION BREATHLESSNESS	POLYURIA POLYPHAGIA POLYDIPSIA	WEIGHT LOSS	PEDAL OEDEMA	PRURITIS VULVA	DIABETIC FOOT	DIMINISION OF VISION
1	1	2	2	0	2	2
1	1	2	2	0	2	1
1	1	1	2	1	2	1
2	2	1	2	1	2	2
2	1	2	2	0	2	1
1	2	2	2	0	2	2
2	2	2	2	0	2	0
2	2	2	2	0	2	2
1	2	2	2	0	2	0
1	1	1	2	0	2	2
2	2	2	2	0	2	2
1	2	1	1	0	1	0
1	2	2	2	0	2	2
1	2	2	2	0	2	2
2	2	2	2	0	2	2
1	1	2	2	0	2	2
2	2	1	1	0	1	0
2	2	2	2	0	2	2
1	2	2	2	0	2	0
1	2	1	1	0	2	0
1	1	2	2	0	2	2
1	2	1	1	0	1	0
1	2	2	2	0	2	2
1	2	1	1	0	2	0
2	2	2	1	0	2	2
1	2	2	2	0	2	2
1	2	2	2	0	2	1
2	2	2	2	0	2	2
2	2	2	2	0	2	2
1	2	1	1	0	2	0
2	2	2	2	0	2	2
2	2	2	2	0	2	2
2	1	1	2	0	2	2
1	2	2	2	0	2	2
2	2	2	2	0	2	2
2	2	2	2	0	2	0
1	2	2	2	0	2	1
2	2	2	2	0	2	2
2	2	1	2	0	1	0
2	2	2	2	0	2	2

1	2	2	2	0	2	2
2	2	2	2	0	2	2
2	2	1	1	0	1	0
1	2	1	1	0	1	0
2	1	2	2	0	2	2
2	2	2	2	0	2	2
2	2	1	1	0	1	0
2	1	2	2	0	1	2
2	2	2	2	0	2	2
2	1	2	2	0	2	2
1	2	2	1	0	2	2
2	2	2	1	0	2	2
2	2	2	2	0	2	2
2	2	2	2	0	1	0
1	2	2	2	0	2	2
2	2	1	1	0	1	0
2	2	2	2	0	2	2
2	2	1	2	0	2	0
2	2	2	2	0	2	2
2	2	1	1	0	1	0
2	1	2	2	0	2	2
2	2	2	2	0	2	0
2	2	2	2	0	2	1
2	2	2	1	0	1	2
2	2	2	2	0	2	2
2	2	2	2	0	2	2
2	2	1	1	0	1	0
2	2	2	2	0	2	2
1	2	2	1	0	2	2
2	1	2	2	0	2	2
2	2	1	2	0	1	0
1	1	2	2	0	2	2
2	2	1	1	0	1	0
2	2	2	1	0	2	0
1	2	2	2	0	2	2
2	2	2	2	0	2	2
1	2	1	1	0	2	0
1	2	2	2	0	2	2
2	2	2	2	0	2	2
1	1	2	2	0	2	2
1	2	1	1	0	1	0
1	1	2	2	0	2	2
2	2	2	2	0	2	0
2	2	2	2	0	2	0
1	2	2	2	0	2	0
1	1	2	2	0	2	2
1	2	2	2	0	2	0
2	2	2	2	0	2	1
1	2	2	2	0	2	2
2	2	1	2	0	2	0
2	2	2	2	0	1	1
2	2	2	2	0	2	2

2	2	2	2	0	2	2
1	1	2	2	0	2	2
2	1	2	2	0	2	2
2	2	1	1	0	2	0
1	2	2	2	0	2	2
1	2	1	1	0	2	0
1	2	2	2	0	1	2
2	2	1	2	0	2	0
2	2	2	2	0	2	2
1	2	2	2	2	2	2
2	2	2	2	2	2	0
1	1	1	2	2	2	2
1	2	2	2	1	2	2
2	2	2	2	2	2	0
1	2	2	2	2	2	0
1	2	1	2	2	2	0
2	2	2	2	1	2	0
2	2	2	2	2	2	2
2	2	2	2	2	2	0
1	1	1	2	1	2	2
2	2	2	2	2	2	2
2	2	2	2	2	2	2
2	2	2	2	1	2	2
2	1	2	2	2	2	2
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2	2	2	2	2	1	0
2	2	2	2	1	2	2
2	2	2	2	2	2	2
2	2	2	2	2	2	0
1	2	2	2	1	2	2
2	1	2	2	2	2	2
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1	2	1	2	2	2	0
2	2	1	2	1	2	2
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2	2	2	2	2	2	2
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1	2	2	2	2	2	2
1	2	2	2	2	2	2
2	2	2	2	1	2	2
2	2	2	2	2	2	0
2	2	2	2	1	2	0
1	2	2	2	2	2	1
2	1	2	2	1	2	2
1	2	2	2	1	2	2
1	2	2	2	2	2	0
2	2	2	2	2	2	2
2	1	2	2	1	2	2
1	2	1	2	1	2	0
2	2	2	2	2	2	2
2	2	2	2	2	2	2

2	2	2	2	2	2	2
2	2	2	1	2	2	0
2	2	2	2	1	2	0
1	2	1	2	2	2	2
2	2	2	1	1	1	2
2	2	1	2	2	1	0
1	2	2	2	2	2	2
2	2	2	2	1	2	2
2	2	2	1	2	2	2
2	2	1	1	2	1	0
1	2	2	2	2	2	0
2	2	2	2	1	2	2
1	2	2	2	1	2	0
2	2	1	1	2	1	0
2	2	2	2	1	2	2
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2	2	1	2	0	2	2
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2	2	2	2	2	2	2
2	2	1	2	1	2	2
2	2	2	2	2	2	2
1	2	2	2	1	2	2
2	2	1	2	1	2	2
1	2	2	2	2	2	2
2	2	2	2	2	2	2

ACUTE COMPLICATION	CAD / MI	HT	PVD	SMOKING	ALCOHOL	PR	BP(mean of 6 readings)	POSTURAL BP DROP
3	2	2	2	2	1	98	4	1
4	2	2	2	2	2	96	2	1
0	2	2	2	2	2	90	0	2
0	2	1	1	2	2	88	1	2
1	2	2	2	2	2	98	1	2
0	1	1	2	2	1	94	0	2
0	1	1	2	2	2	84	2	2
0	1	2	2	1	2	86	3	1
0	1	1	2	1	1	90	2	2
0	2	1	2	2	2	94	2	1
0	2	2	1	2	2	86	1	2
0	1	1	1	1	1	82	2	2
0	1	2	2	1	2	76	1	2
0	1	2	2	1	2	76	0	2
0	2	2	2	2	2	92	1	2
0	1	2	2	2	1	98	2	2
0	2	1	1	2	2	98	3	1
0	2	2	2	2	2	86	2	2
0	1	2	2	1	2	88	5	2
0	1	2	2	1	1	74	0	2
0	1	2	2	1	2	66	0	2
0	1	1	1	1	1	82	3	1
0	1	1	2	1	2	84	4	2
0	1	1	2	1	1	74	5	2
0	2	2	2	2	2	92	2	2
0	1	1	2	1	2	64	5	1
0	1	2	2	1	2	64	1	2
0	2	2	2	2	1	84	5	2
0	2	1	2	2	2	76	5	1
0	1	2	2	1	2	84	2	2
0	2	1	2	2	2	76	3	1
0	2	1	2	2	1	92	5	1
1	2	2	2	2	2	84	1	2
0	1	2	2	2	1	76	0	2

0	2	2	2	2	2	82	1	2
0	2	2	2	1	2	74	1	2
5	2	2	2	1	1	76	2	1
0	2	2	1	2	2	84	1	2
0	2	2	1	2	2	64	1	2
0	2	2	2	2	2	62	1	2
0	1	2	2	1	2	92	0	2
0	2	1	2	2	1	94	2	2
2	2	2	1	2	2	76	1	2
0	1	2	1	2	2	84	1	2
0	2	2	2	1	1	72	2	2
2	2	2	2	2	2	76	0	2
0	2	1	1	2	2	84	4	1
0	2	1	1	2	2	92	3	1
0	2	1	2	2	2	74	2	2
1	2	2	2	1	2	86	1	2
0	1	1	2	2	2	84	2	2
0	2	2	2	2	2	86	1	2
0	2	2	2	2	2	82	1	2
2	2	2	1	1	2	84	1	2
0	1	2	2	2	2	76	1	2
0	2	2	1	2	2	92	1	2
0	2	2	2	1	2	84	0	2
1	2	2	2	2	2	86	0	2
3	2	2	2	2	2	84	0	2
1	2	2	1	1	2	86	5	2
0	2	2	2	2	2	86	2	2
0	2	2	2	2	1	88	2	2
3	2	1	2	1	2	74	2	1
2	2	2	1	2	2	76	2	1
0	2	2	2	2	2	84	1	2
0	2	2	2	1	2	72	2	1
3	2	2	1	2	2	94	5	2
0	2	2	2	2	2	86	5	1
0	1	1	2	1	2	82	1	2
0	2	2	2	1	2	86	2	2
0	2	2	1	2	1	94	4	1
0	1	2	2	2	2	82	4	1
3	2	1	1	1	2	86	3	1
6	2	1	2	2	2	92	3	1
0	1	2	2	2	2	82	5	1
0	2	2	2	2	2	94	5	1
0	1	1	2	1	2	94	5	1
0	2	1	2	2	2	96	5	2
0	2	2	2	1	2	94	3	1
4	2	2	2	1	1	86	3	2
0	1	2	1	2	2	82	3	1
0	1	2	2	2	2	84	2	2
0	2	1	2	1	2	74	3	1
1	1	2	2	2	2	72	2	2
4	2	2	2	1	2	76	2	2
4	2	2	2	1	1	94	5	1

4	2	2	2	1	2	76	2	2
0	1	1	2	1	2	74	2	1
4	2	2	2	1	2	76	5	1
3	2	2	2	1	2	74	3	2
0	2	2	1	2	2	92	2	1
0	2	1	2	2	2	96	2	2
0	2	2	2	1	2	84	3	1
0	1	2	2	2	1	76	1	2
1	2	2	2	2	2	94	1	1
0	2	1	2	1	2	76	2	2
4	2	2	2	1	2	84	5	2
0	1	2	2	1	2	94	3	1
0	1	1	1	2	2	76	5	1
0	2	2	2	2	2	92	3	1
3	2	2	2	2	2	84	2	2
0	1	1	2	2	2	76	0	2
0	2	1	2	2	2	84	1	2
5	2	1	2	2	2	84	2	2
5	2	1	2	2	2	86	5	1
0	2	2	2	2	2	82	1	2
0	1	2	2	2	2	86	2	2
4	2	2	2	2	2	84	1	2
0	2	1	2	2	2	82	2	2
0	2	1	2	2	2	84	1	2
0	2	1	2	2	2	74	1	2
0	1	1	2	2	2	76	1	2
2	2	1	2	2	2	82	1	2
6	2	1	2	2	2	84	1	2
0	2	2	2	2	2	82	0	2
2	2	2	2	2	2	88	0	2
2	2	2	2	2	2	86	0	2
0	2	2	1	2	2	84	0	2
0	2	2	2	2	2	82	2	2
0	2	2	2	2	2	84	1	2
0	2	2	2	2	2	86	0	2
0	1	2	2	2	2	84	1	2
0	2	2	2	2	2	82	2	2
0	1	1	2	2	2	86	2	2
3	2	1	2	2	2	88	2	2
0	2	1	2	2	2	88	3	1
0	2	2	2	2	2	74	2	2
0	2	1	2	2	2	76	2	2
0	2	2	2	2	2	76	1	2
0	2	1	2	2	2	72	2	2
0	2	1	2	2	2	74	1	2
5	2	1	2	2	2	64	0	2
3	2	2	2	2	2	68	0	2
1	2	2	2	2	2	64	0	2
0	2	2	2	2	2	98	0	2
0	1	1	2	2	2	100	0	2
0	2	2	2	2	2	68	2	2
4	2	2	2	2	2	76	1	2

0	1	2	2	2	2	84	1	2
0	2	2	2	2	2	86	1	2
0	2	2	2	2	2	82	0	2
0	2	1	2	2	2	84	2	2
0	2	2	2	2	2	110	2	1
0	2	2	2	2	2	86	2	2
0	2	2	2	2	2	94	0	2
3	2	2	2	2	2	94	2	1
0	2	2	2	2	2	98	1	2
5	2	1	1	2	2	92	1	2
0	2	2	1	2	2	86	1	2
0	2	2	2	2	2	86	2	1
5	2	2	2	2	2	84	1	2
0	2	2	2	2	2	82	1	2
0	2	2	2	2	2	76	5	2
1	2	2	1	2	2	74	4	1
0	1	1	2	2	2	78	4	1
0	1	2	2	2	2	98	2	2
5	1	1	2	2	2	94	2	1
0	2	1	1	2	2	92	2	2
0	2	2	2	2	2	86	2	1
1	2	2	2	2	2	84	1	2
0	1	2	2	2	2	82	5	2
2	2	2	2	2	2	84	3	1
0	2	2	2	2	2	74	2	2
0	2	2	2	2	2	76	1	2
0	2	2	2	2	2	72	1	2
0	2	2	2	2	2	78	2	1
0	2	2	2	1	2	74	2	2
0	2	2	2	2	2	75	2	1
0	2	2	2	1	2	76	1	2
1	2	2	2	2	2	84	2	2
0	2	2	2	1	2	75	2	1
0	2	2	2	2	2	76	1	2
0	2	2	2	1	1	74	0	2
0	2	2	2	2	2	74	0	1
0	2	2	2	1	1	75	0	2
0	2	2	2	2	2	76	1	2
0	2	2	2	2	2	78	2	2
0	2	2	2	2	2	84	1	1
0	2	2	2	2	2	74	1	2
0	2	2	2	2	2	78	0	1
0	2	2	2	2	2	84	0	2
0	2	2	2	2	2	86	2	1
0	2	2	2	2	2	86	2	2
0	2	2	2	2	2	94	2	2
0	2	2	2	2	2	84	2	2
1	2	2	2	2	2	82	2	1

RETINOPATHY	Hb gm %	BLOOD SUGAR	BLOOD UREA	URINE SUGAR	URINE ALBUMIN	URINE DEPOSITS (PUS CELLS)	24 HRS URINARY PROTEIN (MEAN OF 3 SAMPLES)	Sr.CHOLESTROL
2	10.5	282	39	2+	NIL	2--3	170	275
2	12	306	35	2+	NIL	NIL	190	140
3	9	260	23	2+	NIL	NIL	225	200
1	9.8	328	19	1+	NIL	NIL	256	190
2	8.8	355	45	NIL	NIL	NIL	160	230
1	10.5	178	28	2+	NIL	NIL	196	190
0	11.4	291	34	NIL	NIL	NIL	236	275
2	15.2	212	31	1+	NIL	NIL	176	236
0	10.2	265	24	3+	NIL	1--2	246	117
1	10.3	234	45	2+	NIL	1--2	156	245
1	8.5	343	25	3+	NIL	NIL	123	159
2	9	324	33	2+	NIL	NIL	256	365
2	11	205	35	NIL	NIL	1--2	146	354
2	12	224	24	2+	NIL	NIL	245	289
1	16	225	26	2+	NIL	NIL	268	245
1	14	263	28	NIL	NIL	2--3	256	354
0	12	254	24	1+	NIL	NIL	245	174
2	10	263	29	2+	NIL	1--2	158	165
0	9	324	27	NIL	NIL	NIL	147	254
0	8.5	255	15	1+	NIL	NIL	169	265
1	9.5	245	16	NIL	NIL	NIL	254	354
0	10.5	221	24	2+	NIL	1--2	148	265
2	11.5	265	28	3+	NIL	NIL	168	354
0	8	235	39	NIL	NIL	NIL	157	398
2	10	236	34	1+	NIL	1--2	148	345
2	9	245	36	NIL	NIL	NIL	169	214
3	8	345	26	1+	NIL	NIL	254	234

2	9	234	25	NIL	NIL	NIL	268	125
1	9.5	275	29	1+	NIL	NIL	254	145
0	9.5	310	34	1+	NIL	1--2	156	254
1	9.6	345	15	NIL	NIL	NIL	126	265
1	8.5	224	29	NIL	NIL	NIL	135	284
1	10.5		35	NIL	NIL	NIL	139	256
1	11.5	337	36	NIL	NIL	NIL	248	278
1	9.5	265	34	2+	NIL	1--2	103	226
2	8.5	452	26	NIL	NIL	NIL	254	325
3	9.5	482	18	3+	NIL	NIL	105	254
1	9.5	358	17	NIL	NIL	NIL	278	259
0	9.5	254	16	2+	NIL	1--2	256	268
1	10.5	268	35	NIL	NIL	NIL	265	245
1	11.5	258	48	1+	NIL	NIL	248	268
2	9.5	359	35	NIL	NIL	2--3	128	254
0	10.5	354	16	3+	NIL	NIL	269	226
0	11.5	365	39	NIL	NIL	NIL	268	175
1	10.6	369	31	2+	NIL	1--2	154	268
2	12.6	384	39	NIL	NIL	NIL	146	148
0	13.5	265	28	3+	NIL	NIL	187	165
1	14.5	284	25	NIL	NIL	1--2	198	247
2	10.5	289	24	1+	NIL	NIL	278	269
1	10.4	274	29	NIL	NIL	NIL	245	258
1	10.6	268	27	NIL	NIL	NIL	245	265
3	9.5	247	26	NIL	NIL	2--3	265	247
1	8.5	269	35	NIL	NIL	NIL	187	200
2	9	265	34	1+	NIL	NIL	265	198
2	10	334	26	3+	NIL	1--2	248	234
0	12.5	333	38	NIL	NIL	NIL	149	230
1	11	368	26	1+	NIL	NIL	198	265
0	14	354	35	NIL	NIL	NIL	247	265
1	8	348	34	NIL	NIL	NIL	239	365
0	9.5	369	39	2+	NIL	1--2	287	398
1	8.5	358	35	1+	NIL	NIL	254	347
0	9	348	34	NIL	NIL	NIL	169	398
3	10	369	38	NIL	NIL	NIL	147	245
2	10.5	354	36	1+	NIL	NIL	136	265
1	15	254	34	NIL	NIL	1--2	258	254
3	14.5	268	39	2+	NIL	NIL	146	245
0	12	269	38	1+	NIL	NIL	149	248
1	13.5	247	34	NIL	NIL	NIL	168	365
1	16	269	36	NIL	NIL	NIL	247	354
1	14	248	25	3+	NIL	2--3	268	356
0	15	369	38	1+	NIL	NIL	168	345
1	11	254	41	2+	NIL	NIL	159	369
0	11.6	365	18	NIL	NIL	NIL	267	347
0	9	245	28	1+	NIL	NIL	135	354
1	8.5	298	14	NIL	NIL	1--2	124	368
1	9.5	269	26	1+	NIL	NIL	121	368
0	9.4	248	35	2+	NIL	NIL	246	347
2	9.6	369	36	NIL	NIL	NIL	248	126
1	8.5	247	34	4+	NIL	NIL	245	200

1	10	268	25	2+	NIL	NIL	158	179
0	10.5	347	24	NIL	NIL	NIL	157	365
1	9.5	245	26	3+	NIL	NIL	245	249
0	8.5	269	24	2+	NIL	2--3	158	268
0	14	248	35	NIL	NIL	NIL	268	272
0	12.6	269	35	4+	NIL	NIL	147	295
1	11.2	248	36	3+	NIL	NIL	168	275
0	15.6	269	24	2+	NIL	NIL	268	286
3	14.5	248	15	NIL	NIL	1--2	248	385
1	13.5	269	15	4+	NIL	NIL	159	375
0	14	248	18	3+	NIL	NIL	249	274
3	12.6	269	14	2+	NIL	NIL	256	295
1	12.5	247	14	3+	NIL	NIL	178	374
1	11.2	269	16	NIL	NIL	2--3	214	195
1	11.5	247	18	4+	NIL	NIL	256	185
2	10.5	269	17	3+	NIL	NIL	168	176
0	10	247	25	NIL	NIL	NIL	254	254
1	14	269	14	1+	NIL	NIL	185	398
0	12	356	26	3+	NIL	NIL	238	385
1	9	356	28	1+	NIL	1--2	279	268
0	8.5	265	38	3+	NIL	NIL	175	354
1	7	354	27	NIL	NIL	NIL	236	358
3	7.6	458	39	1+	NIL	NIL	249	368
0	8.5	423	34	3+	NIL	NIL	168	345
1	9.5	458	36	2+	NIL	2--3	215	398
2	9.5	325	35	NIL	NIL	NIL	265	345
0	9	425	39	1+	NIL	NIL	132	275
0	10.5	365	36	3+	NIL	NIL	245	265
0	11.5	248	34	1+	NIL	NIL	269	274
0	10.6	256	32	NIL	NIL	NIL	128	295
1	12.5	348	31	1+	NIL	1--2	147	265
0	14	365	35	3+	NIL	NIL	287	264
1	12	248	36	NIL	NIL	NIL	121	285
3	10	245	38	2+	NIL	NIL	120	275
1	11	365	34	2+	NIL	2--3	256	294
1	15	398	36	NIL	NIL	NIL	232	245
2	10.6	489	32	2+	NIL	NIL	169	216
0	12	458	34	1+	NIL	NIL	274	354
0	13.5	259	36	NIL	NIL	NIL	147	215
2	10	348	32	1+	NIL	NIL	269	285
1	15	368	39	1+	NIL	1--2	258	246
0	10.5	426	38	3+	NIL	NIL	147	274
2	8.5	354	34	2+	NIL	NIL	158	268
1	9	324	38	NIL	NIL	NIL	136	245
0	9.5	368	34	NIL	NIL	2--3	248	274
1	9.5	364	38	NIL	NIL	NIL	239	245
0	9.4	364	25	NIL	NIL	NIL	158	245
2	9	314	24	3+	NIL	NIL	165	158
0	12.5	325	27	1+	NIL	NIL	175	256
1	12.5	325	26	3+	NIL	NIL	146	245
0	10	369	26	NIL	NIL	NIL	247	265
1	10	368	25	NIL	NIL	1--2	158	247

2	10.8	347	28	NIL	NIL	NIL	169	185
1	12.6	369	29	NIL	NIL	NIL	269	184
0	12.9	347	17	4+	NIL	NIL	248	145
0	8	368	14	2+	NIL	NIL	156	261
3	9	325	19	1+	NIL	2--3	269	140
2	10	365	35	NIL	NIL	NIL	147	298
1	8	321	34	NIL	NIL	NIL	245	285
0	8	369	39	1+	NIL	NIL	169	296
1	9.5	358	34	NIL	NIL	NIL	256	245
1	8.5	369	15	3+	NIL	NIL	289	358
0	8.5	357	37	NIL	NIL	NIL	264	385
2	7.6	324	35	NIL	NIL	1--2	247	396
1	7.6	369	36	2+	NIL	NIL	251	374
2	9.5	354	34	1+	NIL	NIL	236	284
0	8.5	368	25	NIL	NIL	2--3	125	259
0	9.5	345	45	NIL	NIL	NIL	149	348
2	10.6	369	41	4+	NIL	NIL	269	287
1	10.7	358	46	3+	NIL	NIL	245	289
0	11.9	369	28	2+	NIL	NIL	145	274
1	12.6	348	26	4+	NIL	NIL	214	296
1	14.6	368	25	NIL	NIL	NIL	147	348
1	13.5	348	35	4+	NIL	1--2	145	175
0	14.5	358	39	2+	NIL	NIL	136	185
0	12.5	256	38	NIL	NIL	NIL	248	195
2	11.5	356	34	2+	NIL	2--3	269	165
0	10.5	245	48	NIL	NIL	NIL	128	175
0	9	265	15	3+	NIL	NIL	156	395
2	8.5	248	36	NIL	NIL	NIL	269	245
2	7.5	465	25	NIL	NIL	NIL	147	195
0	14.5	458	27	2+	NIL	NIL	247	175
1	12.5	498	29	NIL	NIL	1--2	187	185
1	12.5	245	26	2+	NIL	NIL	147	165
1	11.5	354	31	4+	NIL	NIL	258	200
1	10.5	365	35	2+	NIL	2--3	264	186
1	12.5	248	15	2+	NIL	NIL	158	198
1	10.5	256	34	NIL	NIL	NIL	148	182
1	10.5	258	35	3+	NIL	1--2	269	245
1	11.5	358	38	NIL	NIL	NIL	247	169
1	10	365	38	3+	NIL	NIL	145	175
2	9.5	248	35	NIL	NIL	NIL	258	186
1	9.6	236	34	NIL	NIL	NIL	247	195
1	9.4	245	39	NIL	NIL	1--2	265	190
2	8.6	368	34	NIL	NIL	NIL	169	175
1	8.4	367	36	NIL	NIL	NIL	214	169
1	10.5	245	34	NIL	NIL	NIL	187	241
1	11.5	368	36	NIL	NIL	NIL	214	198
1	10.5	265	38	1+	NIL	1--2	258	176
1	11.6	365	34	4+	NIL	NIL	157	175
2	8.5	458	31	NIL	NIL	NIL	214	215
2	9.5	368	39	NIL	NIL	NIL	269	189
2	10.5	352	25	3+	NIL	NIL	168	215
1	9.5	321	35	NIL	NIL	1--2	269	235

	1	12.5	326	24	NIL	NIL	NIL	247	175
	2	12.6	356	28	NIL	NIL	NIL	158	198
	1	14	245	39	NIL	NIL	1--2	147	210

TGL	HDL	VLDL	LDL	ESTIMATED GFR BY **MDRD** FORMULA	STAGE OF CKD	SERUM CREATINE	height	weight	waist circum
156	42	42	91	47	3	1.5	153	40	75
185	41	37	170	45	3	1.8	171	69	84
165	42	40	66	47	3	1.6	156	67	86
147	39	50	76	54	3	1.4	159	42	82
285	43	83	121	86	2	1	167	68	84
255	44	51	180	45	3	1.7	157	57	86
286	41	90	138	42	3	1.8	169	50	76
271	42	35	63	65	2	1.9	159	48	84
159	35	70	153	50	3	1.6	167	68	116
210	40	60	100	110	1	0.8	149	65	102
281	48	62	155	57	3	1.4	162	54	85
273	46	24	120	99	1	0.9	157	75	96
178	39	57	151	49	3	1.9	168	61	117
120	44	46	130	82	2	1.7	168	53	95
273	42	49	118	106	1	0.8	168	45	87
100	46	37	87	91	1	0.9	159	62	84
168	47	80	71	46	3	1.6	164	68	86
198	45	64	190	48	3	1.6	151	58	75
291	37	60	140	41	3	1.8	169	57	85
281	40	70	128	82	2	1.8	168	47	83
126	42	85	103	43	3	1.7	164	49	84
145	46	51	42	47	3	1.6	164	67	92
283	45	73	148	74	3	1.1	167	58	86
283	48	48	152	50	3	1.6	168	67	99
168	41	85	139	45	3	1.6	157	45	81
158	45	71	43	61	2	1.3	162	65	95
182	46	75	244	67	2	1.2	169	58	76
189	48	48	271	50	3	1.5	158	45	94
193	38	86	274	102	1	0.8	158	41	87
279	35	75	294	49	3	1.6	169	49	106
275	42	68	237	58	3	1.4	168	75	119
178	42	85	182	42	3	1.8	167	69	82
196	41	82	275	81	2	1	167	49	83
214	41	67	147	52	3	0.5	167	71	76
189	38	45	162	48	3	1.6	169	46	81
293	40	93	279	159	1	0.6	159	63	86
175	43	95	127	44	3	1.7	162	59	73
135	43	52	70	49	3	1.5	145	42	86
286	46	45	163	127	1	0.7	166	54	94
289	39	68	92	47	3	1.6	162	68	112
185	48	62	225	41	3	1.8	165	51	95
145	42	52	160	178	1	0.5	159	59	93
195	35	51	162	37	3	1.9	159	49	75
271	48	36	181	46	3	1.8	157	51	84
296	42	42	281	73	2	1.1	168	61	75
178	42	95	217	153	1	0.6	175	68	88
169	46	65	243	107	1	0.8	164	62	85
268	40	82	143	39	3	1.8	143	47	84
275	42	52	262	133	1	0.7	168	69	76
165	41	72	221	40	3	1.9	164	75	75
175	41	95	209	49	3	1.5	157	44	84
128	43	84	297	53	3	1.2	154	40	76
168	43	84	242	54	3	1.5	169	58	109
273	42	85	218	48	3	1.6	158	64	84
195	42	72	232	46	2	1.6	167	49	74
188	39	55	120	45	3	1.7	168	67	76
185	39	65	240	54	2	1.4	165	58	76
249	43	68	105	53	3	1.5	169	87	115
275	43	54	271	93	1	0.8	168	65	71
162	37	52	36	41	3	1.9	145	78	76
146	41	35	292	108	1	0.8	167	64	76
175	42	48	54	51	3	1.5	167	59	89
186	42	62	243	102	1	0.8	169	46	72
238	45	43	168	49	3	1.5	157	48	76
186	39	41	46	44	3	1.7	164	48	107
187	45	75	145	196	1	0.5	167	69	94
295	41	85	74	93	1	0.9	167	43	84
135	48	76	160	90	1	0.9	167	49	75
175	42	75	62	55	3	1.5	168	67	72
182	42	71	143	55	3	1.5	159	75	91
192	38	94	233	49	3	1.5	163	43	85
283	41	72	165	110	1	0.8	167	71	76
172	40	72	137	64	2	1.3	162	65	76
286	48	73	107	109	1	0.8	174	65	82
275	40	62	166	66	2	1.2	158	48	94
243	38	76	211	48	3	1.6	158	58	74
182	37	41	194	54	3	1.4	156	46	82
185	41	81	132	84	2	1	167	45	94
186	43	82	179	47	3	1.6	169	43	74
198	40	92	127	51	3	1.5	181	58	86
165	42	51	183	79	2	1.1	158	68	95
187	46	65	183	48	3	1.6	183	59	79
295	42	63	181	41	2	1.8	168	54	85
156	39	93	101	76	2	1.1	175	59	82
198	36	43	306	42	3	1.8	164	61	86
284	48	65	155	67	2	1.9	174	48	117
189	40	84	251	55	3	1.4	159	52	84
247	49	83	199	47	3	1.6	185	47	99
175	42	82	148	49	3	1.5	165	56	86
286	46	84	98	42	3	1.7	160	45	75
276	43	84	168	50	3	1.5	154	59	84

160	35	75	264	69	2	1.8	159	69	80
208	41	92	180	52	3	1.5	169	65	84
189	40	45	202	97	2	0.9	158	67	86
245	40	96	138	35	3	1.8	152	69	106
266	42	62	180	68	2	0.9	164	54	89
262	38	86	246	52	3	1.5	169	69	80
269	39	93	262	70	2	0.9	152	51	80
167	43	56	269	113	1	0.6	158	59	84
258	40	63	231	88	2	0.9	154	51	85
159	41	52	295	130	1	0.6	156	68	84
187	40	82	263	38	3	1.6	168	76	96
295	39	57	295	80	3	1.8	165	66	92
262	38	69	289	70	2	0.9	169	60	90
285	41	52	242	47	3	1.2	168	52	75
158	38	67	180	38	3	1.5	167	66	86
262	42	84	188	28	3	1.9	168	67	95
258	40	82	159	107	2	0.8	159	68	85
243	37	83	172	88	2	1.2	167	53	86
162	38	91	135	106	2	0.9	159	59	96
175	40	68	192	68	2	0.9	169	65	87
168	37	75	153	109	1	0.7	168	60	91
156	40	55	181	79	1	1.9	145	67	93
133	40	82	172	69	2	0.9	145	58	86
262	38	83	183	60	2	1.5	168	64	73
285	40	56	180	57	3	1.6	157	62	74
182	40	85	220	58	3	1.6	145	58	106
285	40	42	100	37	3	1.8	159	58	89
245	39	68	178	58	3	1.5	168	60	83
165	42	92	150	57	3	1.5	149	64	80
232	40	62	151	67	2	0.9	158	57	84
295	39	53	150	108	1	0.6	156	67	109
282	39	66	142	118	1	0.6	158	66	91
192	40	92	160	156	1	0.5	167	67	86
262	40	67	167	178	2	0.8	158	67	85
189	41	83	182	98	1	0.8	143	50	75
289	39	95	48	40	3	1.5	162	68	82
155	40	82	152	30	3	1.6	154	43	85
268	45	68	109	38	2	0.8	157	58	76
226	38	83	153	34	2	0.9	169	58	94
275	40	86	169	142	1	0.6	153	56	105
186	40	68	69	38	3	1.6	158	67	185
286	40	94	80	156	2	0.8	152	60	86
169	41	71	33	41	3	1.4	154	55	87
215	36	75	150	107	1	0.6	158	65	84
147	42	54	44	81	2	0.8	157	71	82
283	41	87	170	51	3	1.2	153	68	106
158	40	56	189	78	2	0.8	157	69	87
263	43	46	207	55	3	1.1	168	59	82
273	40	58	147	38	3	1.5	154	54	107
168	40	68	250	84	2	0.8	157	68	89
256	42	62	281	48	3	1.2	153	67	82
136	36	85	275	38	3	1.5	152	61	106
268	42	65	267	69	2	0.9	158	67	85

Sex- male -1, female-2

Type of diabetes mellitus - type 1 DM- 1, type 2 DM- 2

Treatment – 0- recently diagnosed, 1- on regular treatment 2- no treatment

CHEST PAIN PALPITATION BREATHLESSNESS- 1-yes, 2- no

POLYURIA POLYPHAGIA POLYDIPSIA- 1-yes, 2- no

WEIGHT LOSS- 1- yes, 2- no

PEDAL OEDEMA-1-yes, 2- no

PRURITIS VULVA--1-yes, 2- no

DIABETIC FOOT--1-yes, 2- no

DIMINISION OF VISION—0- cataract ,1-vision loss, 2- no vision loss

ACUTE COMPLICATION - 1- diabetic keto acidosis, 2- hypoglycemia,

3-cereberovascular accident, 4- myocardial infarction, 5- acute coronary syndrome,

6-hyperosmolar coma

CAD / MI--1-yes, 2- no

HT--1-yes, 2- no

PVD--1-yes, 2- no

BP (mean of 6 readings) 1- 130-139 / 85-89, 2- 140—150/ 90—99,

3- 160 -179 / 100-109, 4- > 180 / >110, 5- > 140 / < 90

POSTURAL BP DROP

RETINOPATHY- 0 – not visualized, 1- normal, 2- back groundretinopathy,

3- proliferative retinopathy

Hb GRADE- 1->12 gm% , 2-< 12 gm%

STAGE OF CKD (GFR) 1- >90ml/hr, 2— 60- 89 ml/hr, 3- 30 -59 ml/hr,

4- 15-29 ml/hr, 5- < 15 ml/hr.

GLOSSARY

ACR- ALBUMIN CRETININE RATIO
ARB- ANGIOTENSIN RECEPTOR BLOCKER
AER— ALBUMIN EXCRETION RATE
AGE- ADVANCED GLYCAN END PRODUCTS
ACE- ANGIOTENSIN CONVERTING ENZYME

BMI- BODY MASS INDEX

CAD - CORONARY ARTERY DISEASE
CVD- CARDIO VASCULAR DISEASE
CURES- CHENNAI URBAN RURAL EPIDEMOLOGY STUDY
CKD – CHRONIC KIDNEY DISEASE
CTGF- CONNECTIVE TISSUE GROWTH FACTOR

DN— DIABETIC NEPHROPATHY
DCCT- DIABETES CONTROL AND COMPLICATION TRIAL
DAG- DIACYL GLYCEROL
DKD- DIABETIC KIDNEY DISEASE

ESRD- END STAGE RENAL DISEASE

GFR- GLOMERULAR FILTERATION RATE
GLUT- GLUCOSE TRANSPORTER

IGT- IMPAIRED GLUCOSE TOLERANCE

MA- MICRO ALBUMINURIA
MDRD- MODIFIED DIET AND RENAL DISEASE
MAPKS- MITOGEN ACTIVATED PROTIEN KINASES

NON-STEMI- NON- ST ELEVATION MYOCARDIAL INFARCTION

PKC- PROTEIN KINASE C
PVD-- PERIPHERAL VASCULAR DISEASE

RAGE- RECEPTOR FOR ADVANCED GLYCAN END PRODUCTS
RAS- RENIN ANGIO TENSIN SYSTEM

UKPDS- UNITED KINGDOM PROSPECTIVE DIABETS STUDY

VEGF- VASCULAR ENDOTHELIAL GROWTH FACTOR